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PHILADELPHIA

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# THE SURGICAL CLINICS OF NORTH AMERICA

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PHILADELPHIA NUMBER

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## *SYMPOSIUM ON RECENT ADVANCES IN GYNECOLOGY AND OBSTETRICS*

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### FOREWORD

It has been a pleasure as well as a responsibility to direct this symposium on obstetrics and gynecology for the Philadelphia number of the *Surgical Clinics of North America*. The task has been pleasant because of the generous response of my associates, who have made worthwhile contributions through the sacrifice of valuable time and energy on their part. The selection of pertinent subject matter carries with it decided responsibility.

In choosing the subjects for discussion, we have endeavored to present various obstetric and gynecologic problems that may well be considered controversial in some respects at least. Those contributing have been selected because of their experience and ability in the specific fields mentioned, and because of their realistic, but withall dispassionate, approach to the questions at issue. While the majority of the authors are members of the staff of the Department of Obstetrics and Gynecology at Jefferson Medical College and Hospital, it has been our good fortune to have been able to enlist for this symposium outstanding departmental representatives from the University of Pennsylvania (medical and graduate schools and hospitals), Hahnemann Medical College and Hospital, and from the School of Medicine and Hospital of Temple University.

We believe that this symposium adequately covers the field of early diagnosis of uterine carcinoma as well as the controversial issues at stake today with respect to its management. The relationship of uterine fibroids to carcinoma, especially with regard to treatment, is an associated problem of vital interest and has a rightful place among the topics listed in these "Clinics". Surgery in uterine displacements and the role it plays in pelvic inflammatory disease are purposefully discussed, as

are those banes of postoperative morbidity and mortality, thrombophlebitis and phlebothrombosis. Operative necessity with respect to the pregnant state is always with us.

It is with a keen sense of gratitude and appreciation of their efforts that we present the contributions of our Philadelphia colleagues, hoping for them an agreeable reception.

LEWIS C SCHEFFEY, M D , Sc D (Hon )

## NEWER METHODS IN THE MANAGEMENT OF THE ABNORMAL CERVIX

GEORGE A. HAHN, M.D., F.A.C.S.\*

To the gynecologist the cervix is probably the most important structure in the human body. Abnormalities of the cervix constitute a large proportion of the conditions which are seen in the physician's practice. During the years 1943 to 1947, 4138 women, presumably without presenting symptoms, were examined in the Cancer Prevention-Health Maintenance Clinics sponsored by the Donner Foundation in Philadelphia, with the cooperation of the Philadelphia County Medical Society. Of these 4138 women, 2143 were found to have abnormalities of the cervix, sufficient to warrant the examining physician to request specific therapy. It would be wise for every physician to consider every lesion of the cervix as a potential cancer. If this is done the cervix will receive the attention which it merits.

### ANATOMY AND PHYSIOLOGY

An understanding of the anatomy and physiology of the cervix is essential to the intelligent treatment of abnormalities of the cervix.

The uterine cervix is a fibromuscular structure which is an integral part of the uterus. It begins at the so-called "isthmus" of the uterus where the type of mucosa and myometrium change definitely in character. During pregnancy the uterine cervix does not undergo marked evolutionary changes and merely serves as a barrier to protect the inside of the uterus. During the nonpregnant state the cervix serves as a structure to which the supports of the uterus are attached. It protects the inside of the uterus itself, serves as a passage for the spermatozoa from the vagina and its secretion maintains a normal vaginal moisture.

As mentioned, the type of *mucous membrane* changes abruptly near the isthmus of the uterus. The endocervical tissue, extending from the internal os, is thrown into folds presenting a large surface with a definite type of columnar epithelium and a number of racemose glands which extend deeply into the body of the cervix. The endocervix becomes confluent with the vaginal portion of the cervix at the external os—the *squamocolumnar junction*. The *vaginal portion* of the cervix is that part

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which extends into the vaginal canal and is covered by a continuation of the so-called "mucous membrane" which covers the vagina, and normally contains no glands.

The *external os* of the cervix in the nulliparous female is a circular structure about 5 mm. in its transverse diameter, and quite regular in outline. Its circumference marks the area where the epithelium changes from the columnar to the squamous type. The size and shape of the external os of the cervix may be influenced by various factors such as labor, trauma, infection and congenital misplacements of endocervical mucous membrane. The *internal os* is circular, about 1 mm. in diameter, and rarely changes its shape. It must be remembered that the endocervix undergoes cyclic changes during the menstrual cycle which are as definite as those observed in the endometrium.

The glands of the endocervix secrete mucus which has an alkaline reaction. The secretion is moderate in amount and fills the cervical canal and some of the secretion is deposited in the vaginal canal. Normal cervical secretion is bacteriologically sterile and contains degenerated epithelium and some mucous cells and glycogen.

Because the life cycle of the female is divided into three stages, and because features which characterize one period of life may be changed in another, it is important to know that before puberty the endocervix is a rudimentary structure and is not fully developed. After the menopause the cervix undergoes involutionary changes and approaches closely the undeveloped structure present before puberty.

### CHRONIC CERVICITIS

Acute cervicitis does not require surgical treatment and therefore will not be considered in this paper.

The term "chronic endocervicitis" denotes gross and microscopic changes in the mucosa of the endocervix. As changes from the normal occur in the mucosa, secondary changes are brought about in the entire cervix. The condition known quite generally as chronic endocervicitis is really a chronic cervicitis.

In a fairly high percentage of patients who have had acute cervicitis due to infection from the gonococci, streptococci or associated with the trauma of labor and delivery, the disease may progress to a chronic state. The symptoms would include *leukorrhea*, *backache* and *lower abdominal pain*. Less commonly, *menorrhagia*, *metrorrhagia*, *dyspareunia*, *dysmenorrhea*, *dysuria*, *pruritus* and *sterility* may be associated with this condition.

**Etiology.**—Gonorrhea may be the cause of this lesion, although this may be difficult to prove bacteriologically. Usually chronic cervicitis

follows injuries due to childbirth. More rarely, instrumentation, the use of stem pessaries or even possibly the use of vaginal tampons for absorption of the menstrual flow, may be implicated. Whatever the cause may be, the bacteriologic agent will usually be one of the streptococcus or staphylococcus groups. Invariably there will be an alteration in the vaginal pH from its normal of 4.5.

**Clinical Picture.**—It may be difficult to demonstrate minor degrees of endocervicitis if the vaginal portion of the cervix appears normal. The changes noted in the appearance of the cervix are important; all changes from the normal are significant and must be recognized. There may be slight variations in the color of the cervix and the canal of the cervix may appear cyanotic and edematous. *The canal is oftentimes stenosed.* When the canal is dilated it will seem granular and often soft. There will be an increased amount of cervical secretion and oftentimes it is cloudy in appearance. In cases of endocervicitis it is well to make a stained smear or a hanging-drop preparation of the cervical secretion and examine it under the microscope. The presence of pus cells in the secretion is proof that the cervix is not normal. It is important that the specimen be not secured near the time of menstruation in order to reduce the chance of uterine contamination. Care in technic will preclude contamination from the vagina.

**EROSION.**—Clinically, erosion presents itself as a bright red area immediately surrounding the external os. The normal epithelial covering is gone and the erosion has a rather granular appearance. It is soft to palpation. Usually there is a plug of purulent material present in the os. Occasionally there may be slight bleeding brought about by manipulation.

The erosion may be *congenital*—the so-called “pseudo-erosion” that is found oftentimes to be the cause of leukorrhea in nulliparous or virginal women. It is felt that this lesion is the result of misdevelopment and probably bears no relationship to the usual inflammatory type of erosion. The portion of the cervix which is affected by the congenital type of erosion is covered by a layer of columnar epithelium rather than by squamous epithelium, because the primary downgrowth of tissue present at birth has never regressed.

In the *acquired* erosion, in addition to the replacement of the squamous epithelium by columnar there is usually round-cell infiltration present and there may be even actual loss of epithelium. It is a misnomer to call an erosion an ulcer since true gross ulceration does not occur unless due to carcinoma, syphilis or tuberculosis.

The *simple* erosions are those in which the area is fairly smooth and bright red. The single layer of columnar epithelium with few or no glands

allows the underlying vascular tissue to show through, giving the typical red appearance.

*Papillary erosions* are those in which the downgrowth of the glandular epithelium has been more extensive so that the area is more irregular and rougher to the touch.

*Follicular erosions* are a later stage of the papillary process in which the irregularity of the cervix is more prominent

When the simple, papillary or follicular erosion has healed to some extent, the openings in the cervical glands may become plugged or covered over so that retention or nabothian cysts form. These cysts may feel as hard as lead pellets in the cervix. Ordinarily the mucus in these cysts is clear and stringy but in the presence of infection the cyst may be corn-yellow in appearance. Occasionally these cysts may become as large as a walnut or even larger and may simulate cervical myoma or carcinoma.

**ECTROPION, EVERSION.**—*Ectropion or eversion of the cervix* may occur as a result of deep laceration of the cervix with formation of scar tissue so that the cervical lips are rolled outward, everting the cervical mucosa. When this occurs the cervix is patulous, enlarged and the typical "fish-mouth" appearance results.

**LEUKOPLAKIA.**—*Leukoplakia* is the term applied to gray-white, thickened areas which may be seen on the cervix. If the patch is rubbed off it will return in a short while. We rarely see true leukoplakia of the cervix. It must be remembered that certain types of syphilis of the cervix may present a leukoplakic appearance.

**LACERATIONS OF THE CERVIX**—*Lacerations of the cervix* are found in the large majority of women who have borne children. In most instances superficial lacerations heal spontaneously. The deeper tears usually occur only with operative interference at the time of delivery. Injudicious use of pituitrin may bring about severe lacerations. Delivery through an incompletely dilated cervix, particularly in the primipara, is often associated with deep tears of the cervix. Occasionally a cervical tear may result because of a hasty instrumental dilation of the cervix prior to endometrial curettage.

Tears may occur anywhere in the cervix and may be single or multiple and may be limited to the cervix or may extend into the lower uterine segment.

The type of laceration is important since the splitting of the cervix may produce a progressive eversion of the mucosal elements of the cervix. The important symptoms are due, not to the laceration itself, but to the infection superimposed upon the laceration. The infected, inflamed laceration is, of course, just another type of chronic cervicitis.

**HYPERTROPHY OF THE CERVIX.**—When the cervicitis is of long standing and the severity of the condition increases, hypertrophy of the cervix invariably results because of the cyst formation that has taken place and because of the replacement fibrosis that results.

Depending upon the degree of cervicitis that is present, there may or may not be any symptoms referable to the pelvic region. The simple erosion may only be detected on routine pelvic examination of the woman who is symptom-free. Occasionally the only complaint of these patients is sterility. Usually, however, the symptoms of leukorrhea, backache and lower abdominal pain may be elicited by careful questioning in any patient with a marked degree of cervicitis.

**Treatment of Chronic Cervicitis.**—The treatment of the cervical lesions, erosion, eversion, cervicitis and laceration, must take into consideration the underlying pathology of the condition. The methods of treatment will be discussed under one heading since the lesions frequently overlap and sharp lines of demarcation cannot always be made.

The most important consideration in the management of cervicitis is whether or not beginning cancer is present. It would certainly appear that there is a distinct relationship between the occurrence of carcinoma of the cervix and cervicitis. If cancer is present the diagnosis must be made at the earliest possible moment so that successful treatment may be started. If cancer is not present, elimination of the cervicitis should prove to be an important factor in preventing the first malignant change.

Before any plan of treatment is embarked upon, a careful pelvic and rectal examination must have been done. In addition to the usual bimanual examination it is essential that the cervix be exposed completely and be examined with the aid of adequate light. We prefer to use a head-mirror so that the entire cervix is well illuminated. When it is necessary to examine a virginal patient in whom it is difficult to utilize the usual virginal speculum satisfactorily, we have found the Kelly cystoscope to be a valuable adjunct in exposing the cervix for examination. If there is any doubt about the findings, examination under anesthesia is of course recommended. The Papanicolaou method of study of the cervical or vaginal secretion, utilizing the suction type of pipette or the Ayre type of cervical spatula, is used when indicated. On the gynecologic ward service at Jefferson Hospital all patients have the benefit of vaginal cytologic study by the Papanicolaou method prior to any operative procedure.

In the past the local application of powders, pastes and caustics such as silver nitrate was popular in the management of cervical erosions and the like. We do not favor the use of such methods in the treatment of the abnormal cervix.



**MINOR LESIONS**—For the patient with a minor degree of endocervicitis with its usual associated cervical stenosis, satisfactory treatment, which includes adequate drainage of the cervical canal and destruction of the diseased endocervical tissue, may be carried out in the office. We use a 1:1000 aqueous solution of zephiran to cleanse the cervix prior to any operative manipulation. After the cervix has been effectively cleansed the external os may be easily dilated with a pair of uterine dressing forceps or a small Goodell type of dilator. If, after six to eight weeks of adequate dilation of the cervix, the endocervicitis is still present, especially if there is an associated eversion, the diseased tissue should be destroyed by coagulation or cauterization with the electric cautery. For the small area that needs to be treated the nasal tip cautery is quite adequate, and the treatment necessary consists of a few linear strokes about  $\frac{1}{8}$  inch deep and  $\frac{1}{2}$  inch apart through the everted area, including the edge of the external os. Anesthesia is not necessary and the whole treatment should be completed at once. If the coagulation current is available, it is more convenient and a little more adequate. Immediately after treatment the vaginal discharge increases and there may be slight vaginal bleeding. Ordinarily, the cervix is healed in three to four weeks. This type of treatment is not applicable for larger lesions of the cervix and of course should never be used when there is any suspicion of cancer, since no biopsy is taken. If additional treatment is given, six to eight weeks should elapse so that healing is complete.

For the patient who has developed a minimal eversion and or erosion subsequent to delivery, cauterization or coagulation of the cervix should be done. The method is the same as that already described. The treatment should not be instituted for at least six weeks after delivery since normal involution of the pelvic organs frequently causes the diminution or even complete disappearance of the supposed erosion of the cervix.

**EXTENSIVE LESIONS.**—For the patient who has a lesion more extensive than the minor endocervicitis or the minimal eversion and/or erosion which is discovered at the time of the first postpartum visit, a different approach must be made.

The policy on the gynecologic service at Jefferson Medical College Hospital is as follows: All patients with diseased cervixes are admitted to the hospital and the usual complete preoperative studies are performed including a complete blood count and sedimentation rate. We feel that surgical treatment of the cervix should not be undertaken in the presence of an associated pelvic inflammatory disease that is not quiescent. In the presence of an elevated temperature or white count, or an increased sedimentation rate, operation is deferred until the studies are within the

normal range. Vaginal and cervical smears are examined by the Papanicolaou method.

The patient is prepared for operation in the usual fashion and the appropriate anesthesia is used. (Sodium pentothal is being used more and more frequently.) The vagina and cervix are cleansed, the cervix is grasped with a tenaculum and well exposed. After thorough dilation of the cervix with the Goodell dilators, a fractional or differential curettage is performed. The endocervix is first completely curetted and the tissue is placed in a separate receptacle. The endometrial cavity is then curetted, being especially sure that the cornual areas have been thoroughly investigated. Then a *circular* biopsy of the cervix is performed. A scalpel is used and a wide core of cervical tissue including the

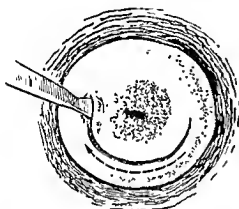


Fig. 390

Fig. 390 —Wide excision of affected tissue, removed by circular biopsy

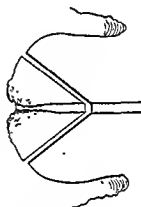


Fig. 391

Fig. 391 —Lateral view of line of excision of affected tissue

endocervix is removed (Figs. 390, 391). The line of excision must be well beyond the cervical lesion. It is oftentimes helpful to grasp the tissue to be removed with Allis forceps before the excision is complete. If this type of procedure is carried out, the area of junction between the stratified squamous epithelium and columnar epithelium will be completely excised. It is considered that most cervical cancers begin in this region.

After the circular biopsy has been completed an *endocervical resection* (conization) is done, using the Bovie endotherm, Hyams electrode, the Crossen electrode or the T. K. Brown modification of the Crossen electrode. The electrosurgical resection adequately controls the bleeding. The circular biopsy is done first so that an adequate amount of tissue may be obtained, without cellular distortion by heat, and so that the all-im-

portant *squamous-columnar junction may be completely removed*. The cone of tissue is cut into several blocks and sectioned for histological examination. It is by doing biopsies of this type that carcinoma in situ may best be discovered.

If the amount of cervical disease present is small, a satisfactory endocervical resection may be done without preliminary circular biopsy, provided that the line of excision is well away from the margin of diseased tissue and provided that the operation is completed rapidly enough so that a minimum of charring of tissue results. If there is any suspicion of cancerous change *we*, of course, precede the endocervical resection by circular biopsy. A firm vaginal packing is usually allowed to remain in place for twenty-four hours after operation to promote hemostasis.

The patient is asked to return for examination about three weeks after operation. At this time it is imperative that the cervix be dilated with a uterine dressing forceps or small Goodell dilator so that annoying cervical stenosis does not develop. It is usually necessary to dilate the cervix for a few months after operation.

When the diseased cervix is unusually hypertrophied or there is marked irregularity in the size of the lips it may not be feasible to perform a circular biopsy and then an endocervical resection. It is usually better to perform a *trachelectomy* when there is hypertrophy of the cervix. We prefer to split the cervix as far up as required, excise the redundant posterior lip of the cervix with a curved incision and then excise the anterior lip of the cervix with a similar incision. Hemostasis is obtained by means of interrupted sutures after which the flaps of vaginal tissue are sutured in place so that a small completely re-epithelized cervix results. The Sturmdorf type of suture may be of aid in approximating the tissues accurately. It is important that the sutures not be tied tightly and that an adequate cervical canal is allowed to remain.

Circular biopsy of the cervix with endocervical resection or trachelectomy may, of course, be performed in conjunction with other gynecologic procedures such as *repair of cystocele or rectocele*.

Occasionally there is a persisting cervicitis in an old cervical stump following supravaginal hysterectomy. The same plan of treatment may be carried out without additional difficulty.

When there is associated uterine or adnexal disease in conjunction with a diseased cervix, not carcinoma, complete hysterectomy is the procedure of choice.

#### CARCINOMA-IN-SITU

The histological appearance of "noninvasive cervical carcinoma" or "intraepithelial carcinoma" has become increasingly familiar to those in-

terested in gynecological pathology. The cellular changes (variability of the size and shape of the cells, frequency of cellular mitoses, loss of normal epithelial stratification) are identical with the changes present in invasive or metastatic cancer. TeLinde has emphasized the frequent occurrence of basal cell hyperactivity in the surface epithelium in intraepithelial cancer (Figs. 392, 393). Carcinoma-in-situ is strictly a histological diagnosis and may mean that the biopsy was taken from the periphery of an advanced cancer, that cancer is present elsewhere in the cervix or that



Fig 392 —Photomicrograph of cervical biopsy taken from patient under observation at the American Oncologic Hospital. Sharp demarcation between abnormal and normal epithelium. Basal cell hyperactivity is demonstrated

only intraepithelial cancer is present and no invasion has as yet taken place.

Clinically, the appearance of true carcinoma-in-situ is not that of cervical cancer. On pelvic examination there may be no apparent abnormality of the cervix. Usually the appearance is that of cervicitis, erosion, eversion, laceration or leukoplakia. Most of these lesions arise at the junction of the stratified squamous epithelium with the columnar epithelium; this point may occasionally be within the cervical canal. The circular biopsy is ideal for removing this region. TeLinde has treated a fairly large group of patients by means of a modified Wertheim operation in which a fairly wide cuff of vagina and a portion of the parametrium is

removed. No gland dissection is done. In younger patients an ovary may be conserved.

At Jefferson Hospital we have had seven patients in whom the diagnosis of carcinoma-in-situ seems tenable. We do not use hysterectomy or irradiation in the treatment. At present any patient in whom a diagnosis of carcinoma-in-situ has been made is subjected to an extensive circular cervical biopsy so that we may be assured that there is no underlying invasive cancer. These patients are placed in a special category and are followed at regular intervals in our "follow-up clinic" by means of pelvic examinations and Papanicolaou smears. So far none of our pa-



Fig. 393 —Same patients as in Figure 392. More marked basal cell hyperactivity with loss of normal stratification.

tients has developed invasive cancer but it is too early to suggest that none of these cases will ever develop invasive cancer.

It should be emphasized that carcinoma-in-situ may be present in the cervix which clinically may appear to be the seat of a benign erosion or cervicitis. There may be no symptoms referable to the cervix itself, although with careful questioning, a history of postcoital spotting may oftentimes be obtained. When the pathological diagnosis has been made, it is imperative that a more radical type of biopsy be performed so that the presence or absence of underlying invasive carcinoma may be determined. We feel that the circular type of cervical biopsy followed by

electrosurgical endocervical resection is an excellent method of detecting early invasive carcinoma or carcinoma-in-situ in an otherwise unsuspected cervix. It is by means such as this that more early cancers will be diagnosed or perhaps prevented.

### CERVICAL POLYPS

Small, fleshy, red pedunculated tumors may arise from the cervical canal or portio. They may often be found on routine examination without any symptoms. Usually intermenstrual bleeding, vaginal discharge or postcoital bleeding is present.

**Treatment.**—Polyps should be removed. If the polyp is small and the entire base is easily visualized, it may be removed in the office by excising the polyp and pedicle and cauterizing the base. Usually, however, the base cannot be completely visualized and there is an associated cervicitis and erosion. In this event the patient should be hospitalized and after thorough cervical dilation under anesthesia the polyp may be removed. A curettage must accompany the polypectomy and it is usually necessary to perform an endocervical resection at the same time to correct the associated cervicitis. All polyps, after removal, should of course be examined histologically since occasionally they are malignant. An endometrial polyp or pedunculated uterine myoma may give the appearance of a cervical polyp. When intermenstrual bleeding is associated with the presence of a polyp in the older woman we prefer to have radium available at the time of polypectomy and curettage since there may be an associated fundal malignancy.

### CERVICAL MYOMA

Ordinarily, cervical myoma are found in association with uterine myoma and should be treated in conjunction with the uterine tumor. Rarely the tumor may involve the cervix alone. If small it may be treated like the cervical polyp but if it is large complete hysterectomy may be necessary.

### CERVICAL TUBERCULOSIS

Cervical tuberculosis is a rare lesion and is usually found in conjunction with tuberculosis elsewhere in the pelvis. Clinically the appearance is that of carcinoma of the cervix. The diagnosis is made by biopsy. The treatment is complete hysterectomy and removal of both adnexa unless the amount of systemic disease present does not make it seem feasible to submit the patient to this type of surgery.

## CERVICAL SYPHILIS

*Chancre of the cervix is considered a frequent site of the primary lesion* The chancre may be erosive, ulcerative or vegetative. The secondary lesions are usually ulcerative with a rather yellowish discoloration. Leukoplakic changes are common. Tertiary syphilis of the cervix is usually attended by hypertrophy of the cervix with ulceration. Clinically, cervical syphilis must be differentiated from cancer and tuberculosis. In the gynecologic follow-up clinic at Jefferson there is recorded the history of one patient who apparently originally had a cervical lesion which was

usual antisyphilitic regimen, penicillin, arsenicals and bismuth

## THE ABNORMAL CERVIX DURING PREGNANCY

Cervical polyps, cervicitis, cervical erosions, condylomata and decidual reactions may occur in the cervix during pregnancy. The decidual reaction may simulate carcinoma in appearance. As a part of good prenatal care every cervix should be inspected carefully at the first prenatal visit and again at the sixth or seventh month of pregnancy. Any suspected area, erosion or polyp should have the benefit of a biopsy. If the biopsy is carefully taken there is little or no danger of interrupting the pregnancy. Carcinoma of the cervix may occur during pregnancy and the earlier the diagnosis is made the better the chance for successful treatment.

## SUMMARY

1. A description of the anatomy and physiology of the cervix is given
2. The symptoms, etiology and clinical picture of chronic cervicitis are discussed. Congenital erosion, simple erosion, papillary erosion, follicular erosion, nabothian cysts of the cervix, ectropion, eversion, leukoplakia, lacerations and hypertrophy are described.
3. The treatment of the minimal endocervicitis and postpartum "erosion" by cauterization and coagulation is discussed
4. The management of more advanced disease by means of the circular biopsy and endocervical resection is described. The importance of carcinoma is emphasized. The indications are given for trachelectomy and complete hysterectomy.
5. Carcinoma in situ is discussed
6. Cervical polyps, cervical myomas, cervical tuberculosis and cervical syphilis are briefly discussed.

7. The management of the abnormal cervix during pregnancy is briefly outlined

8. The importance of adequate biopsy in the suspected cervix is stressed. It is only by this means that carcinoma in situ and early invasive cancer may be diagnosed. The importance of the treatment of the diseased cervix is emphasized.

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## CONTROVERSIAL FACTORS IN THE MANAGEMENT OF CARCINOMA OF THE CERVIX

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### HISTORICAL SURVEY

UNTIL comparatively recent times, carcinoma of the cervix was considered a hopeless condition. Treatment consisted of supportive measures, palliative curettements and the relief of pain. Astruc, physician to the king of France, in his *Treatise on Diseases of Women*, in 1762, summarized the remedies in use at that time for the so-called cure of cancer. Various preparations of belladonna and hemlock were in vogue because these substances were thought to stay the progress of the disease. Tiberius Lamberger of Groningen was particularly enthusiastic over the efficacy of belladonna and Anthony Storck of Vienna claimed that even large cancers were cured in a month or two by 30 grains of hemlock taken internally each day. Blood letting and drastic purging, the great panaceas of the time, were advocated by everyone who treated cancer. Liquid diet, consisting of broths and the milk of goats and asses, was thought to have a retarding influence on the growth. Local treatment consisted of douching and application of decoctions of nightshade and house leek, solutions of lead, and a broth made from young frogs, crawfish, crabs, snails and earthworms. For the control of bleeding, the juice of plantain and shepherd's purse was injected into the uterus. To this mixture alum was frequently added. Opium by mouth and by local application was widely used for the relief of pain.

At this time few attempts were made to remove the involved structures, although as early as 1560 Andrea della Croce of Venice had performed a hysterectomy with a cautery iron for carcinoma in a prolapsed uterus.

Little progress was made with treatment of carcinoma of the cervix until 1801 when Osiander advocated amputation of the cervix as a curative measure. Sauter, of Constance, in 1821, is credited with performing the first vaginal hysterectomy for cancer and this procedure was widely followed for the next generation. After the advent of anesthesia and im-

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provement in surgical technic, steady progress was made in more complete extirpation of the involved structures by the abdominal route. Great credit is due W. A. Freund who, in 1878, first advocated better exposure of the pelvic organs by use of the position later popularized by Trendelenberg. By 1879, he had performed six hysterectomies for carcinoma of the uterus, three of these patients survived the procedure, one of whom he exhibited twenty-six years later at a gynecologic conference in Breslau. Ahlfeld, in 1880, found the immediate mortality rate from abdominal hysterectomy for cancer to be 73 per cent. Because of this terrific mortality the majority of surgeons returned to the vaginal approach which had been originally proposed by Sauter, and by 1890 approximately 90 per cent of patients survived this procedure.

Because of the obvious advantages to be gained by inspection of the upper limits of the disease other surgeons devoted their attention to further development and refinement of abdominal hysterectomy. In 1896, while Resident in Gynecology at Johns Hopkins Hospital, John G. Clark proposed and performed radical abdominal hysterectomies, removing the uterus, upper vagina, adnexa, the parametria, and the regional lymph glands in one piece. He emphasized the necessity of isolating the ureters in order that the parametria might be removed with relative safety. Rumpf, working independently, advocated a similar operation during the same year. Wertheim, in 1898, developed his radical hysterectomy and to him is due tremendous credit for popularizing this procedure. Widespread adoption of the radical operation furnished abundant material for study of the method of growth of carcinoma of the cervix and firmly established the fact that cure could be obtained surgically only by extirpation of every ramification of the growth. Important information was collected concerning the incidence of involvement of the parametria and regional lymph glands. Thus it was found that the growth had extended beyond the confines of the uterus in approximately two thirds of the cases which preoperatively had been considered to be operable. Even in early cases the regional glands were found involved in 30 to 50 per cent of cases, easily explaining the negligible incidence of cure among those patients who had been subjected to ordinary hysterectomy.

Tausig, in his review of the literature of this period, found the incidence of glandular metastases to be 25 to 33 per cent in Stage I cases, 45 to 50 per cent in Stage II and III cases, and 66 per cent to 100 per cent in extremely late cases. It is interesting to note that the five-year survival rate which obtains whether treatment is surgical or by radiation is almost identical with the absence of glandular involvement.

Following the work of Clark, Rumpf, and Wertheim, radical abdominal hysterectomy became the accepted method of treatment of operable cases

of carcinoma of the cervix throughout the world. Extensive cases were treated palliatively by curettage, cauterization, and the application of a variety of caustic preparations.

After the advent of radium in 1912, the majority of surgeons abandoned operative treatment because of its high immediate mortality. Thirty per cent of Wertheim's first 100 patients failed to survive the operation; the rate was reduced to 15 per cent in his later cases. It is estimated that the average mortality rate of the radical operation during its heyday was approximately 20 per cent, and even this staggering figure does not take into consideration the large number of women who were doomed to invalidism by postoperative urinary and rectal fistulas.

In 1911 Wertheim published the results of his first 500 radical operations. He had operated upon approximately half of the patients who had applied to him for treatment. Of these 42.9 per cent were alive and free from evidence of cancer at the end of five years, giving an absolute survival rate of 18.4 per cent.

Victor Bonney became the outstanding successor of Wertheim in continuing the radical surgical approach. By gradual extension of his criteria of operability, he operated upon 63 per cent of all patients coming to him, with an absolute five-year salvage of 25 per cent. His operative mortality was 14 per cent in 500 cases.

Kelly and Burnham of Baltimore in 1912, initiated the elective treatment of carcinoma of the cervix with radium. The negligible primary mortality, the absence of postoperative morbidity, the almost miraculous immediate response, and the high incidence of apparent cures resulted in its adoption as the treatment of choice in most of the major gynecologic clinics throughout the world.

### RADIATION THERAPY

From 1920 until comparatively recently, radiation in various forms was almost universally accepted as the treatment of choice for all cases of carcinoma of the cervix.

The technic of radiation therapy has undergone a gradual evolution during the past thirty-five years; with increase of knowledge of the physics of radiation and the biologic reaction of tissues to this form of therapy it is rare indeed to see the needless destruction of tissue which was formerly referred to as "the usual radium slough." In most clinics at the present time treatment with high voltage x-ray precedes the local application of radium. This has the fourfold advantage of devitalizing the cancer cells before local manipulation may cause their dissemination, of at least partial sealing of lymphatic channels, clearing up the ever present

local infection, and effecting an amazing restoration of the contracted and distorted anatomical relationships.

At Pennsylvania Hospital we have given 2000 to 2800 roentgens measured in air to one 15 by 15 cm port anteriorly and posteriorly. Recently we have abandoned our earlier goal of giving this arbitrary dosage and now give all the deep therapy which the patient will tolerate, the amount being limited only by the cutaneous and general constitutional reactions. For protection of the bladder and lower bowel a strip of lead

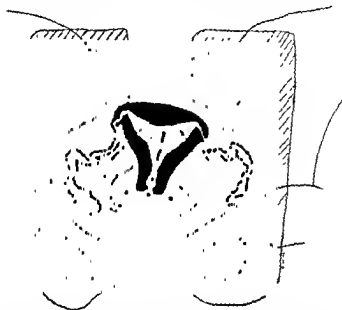


Fig. 394 --Tracing showing usual position of the arc-radium unit. Inner line shows area receiving 10 skin erythema doses, outer line 5 skin erythema doses (Lucas). Solid fields show high voltage x-ray ports to broad ligament and pelvic floor. The 4 cm. lead shield in front and back protects bladder and intestines from additional irradiation. The central zone receives only about half the x-radiation of lateral fields. (Courtesy of Dr. Paul A. Bishop.)

4 cm. wide and 5 mm. thick is placed on the skin in the midline prior to each treatment (Fig. 394). The remaining areas are filtered by 1 mm. of aluminum and 0.5 mm. of copper. Two hundred kilovolts are utilized at a distance of 50 cm. The effective wave length is 0.160 Angstrom unit, and the half value layer is 0.90 mm. of copper. If well tolerated 200 roentgens are administered anteriorly and posteriorly three times each week. In our earlier cases two lateral ports were used but this was discontinued because of the high incidence of fracture of the neck of the

femur following this relatively ineffectual amount of exposure. The addition of the lead strip, which reduces the depth dose to the midline structures by 50 per cent, has diminished the number of both early and late bladder and bowel reactions.

The abdominal and loin ports are often supplemented by a cervical port, the radiation being delivered through an intravaginal cone. Behney, and more recently, Taylor and Twombly, have reported promising improvements in salvage following use of this method, particularly as compared to the use of interstitial needles.

Four weeks after completion of the x-ray cycle the local application of radium is made. Techniques vary widely in minor details but the con-

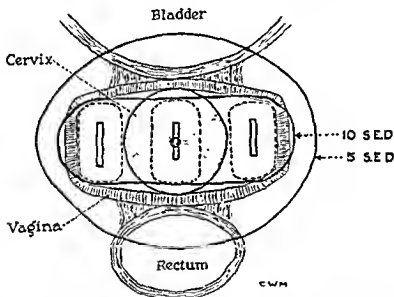


Fig. 395.—Horizontal isodose curves for colpostat with capsule in each lateral fornix, and capsule vertically against cervix. SED. refers to skin erythema dose (After Lucas, 1936)

sensus is to give approximately 6000 milligram hours to the cervical area, including the cavity of the uterus and the bases of the broad ligaments. This dosage will vary upward if small amounts of heavily filtered sources of radiation are used, or downward if larger quantities of radium are utilized. Our own technic (Fig. 395) is to place three 10 mg. capsules into the cervical canal filtered by 1 mm. of platinum. One 10 mg. capsule filtered by 2 mm. of platinum is plated in the vagina anteroposteriorly across the cervix, and a 10 mg. capsule similarly filtered is placed in each side of a colpostat. This technic utilizes a total of 60 mg. of radium which is left in place for a period of 100 hours. The intravaginal portion of the treatment is omitted in those patients who have previously received x-

ray therapy through the vaginal cone. Not infrequently the radium dosage is divided into two applications at an interval of one month. Because of the potent dangers of infection and of injury to the ureters and the uterine vessels we do not use radium needles.

When the cancericidal effects of radium were first understood it seemed quite logical to insert radium needles into cancer-bearing tissue. Because of the difficulty in placing the needles, lack of proper filtration, and excessively long application, fistulas were not infrequent. As a result the use of needles was generally discontinued. A few clinicians still use them with good results. Recently Waterman has renewed interest in this technique by his excellent results, obtaining a 39.3 per cent absolute five-year survival rate in 127 cases, and a relative five-year survival rate of 44.9 per cent in 109 cases treated primarily with needles. In a group of 485 patients treated with needles, only twelve patients developed fistulas.

Considerable controversy exists concerning the value of radiation therapy of cancer which has already extended to regional lymph glands. The late Fred J. Taussig concluded from his own experience and from an extensive review of the subject that radiation therapy did not destroy metastases in lymph glands, and for this reason he developed his technique of lymphadenectomy as an adjunct to full radiation therapy. By this method he was able to increase his five-year salvage from 22.0 per cent to 38.6 per cent in groups of cases of comparable extent (Group II League of Nations Classification).

On the other hand, Morton, who also performs lymphadenectomy in selected cases, found cancer in lymph glands three times more often in patients who had not received x-ray therapy than in a comparable group who had been so treated. This would indicate that present methods of x-ray therapy can destroy cancer in lymph glands. This is further substantiated by the greatly improved salvage reported by many clinicians following the use of modern methods of roentgen therapy (Ward, Schmitz, Miller, Given). Because we believe that x-ray therapy does destroy cancer in lymph glands we have not adopted lymphadenectomy as a routine in our clinic. The benefits of the operation do not seem to us to justify its hazards.

**Results of Radiation Therapy.**—The absolute results of any form of treatment for cancer must be calculated upon the number of patients who are living and free from evidence of cancer after a standard number of years compared to the number of patients who apply for treatment. The relative survival rate is based upon the number of patients who were actually treated. Unfortunately there is such a wide variation in methods of reporting results that comparison of survival rates is extremely difficult. The average absolute five-year survival rate follow-

ing combined radiation therapy as estimated from present day reports is in the neighborhood of 25 per cent.

A fair average of five-year salvage figures for growths apparently limited to the cervix is 75 per cent; for those questionably limited is 50 per cent; for those which have invaded the broad ligaments is 20 per cent; and in the group of cases in which the growth has involved the entire pelvis, the five-year salvage is practically nil. These results reported by a large number of gynecologists and radiologists, are quite comparable with the salvage obtained by such master surgeons as Bonney and Wertheim with the radical operation. The primary mortality is practically nil and urinary fistulas and other untoward postoperative sequellae are rare.

The absolute survival rate at the Pennsylvania Hospital in a group of 130 patients seen from January 1, 1933, to December 31, 1941, was 27.6 per cent. The classification devised by Henry Schmitz has been utilized in our clinic since its inception. His grouping is comprehensive, simple, workable, and is easily remembered. Furthermore, his limitation of Stage I cases to those no larger than one centimeter in diameter places the division between early and late cases at a logical point. In Stage I cases our salvage was 85.7 per cent, in Stage II, 47.3 per cent; in Stage III, 18.2 per cent. In the late (Stage IV) cases there were no five-year survivors. It is interesting to note that these survival rates are in direct proportion to the usually recognized absence of involvement of the regional lymph glands. This clearly brings into focus the necessity of either more effective technics of radiation or the surgical removal of the metastatic glands.

### THE RADICAL SURGICAL APPROACH

Within the past few years Meigs, Taylor, Counsellor, Morton, Carter, and a few others have returned to the Wertheim operation combined with Taussig's lymphadenectomy for the treatment of certain early selected cases. Meigs has recently detailed his reasons for this decision as follows:

"1. If the cervix is removed, there is no chance for recurrence in it.

"2. If the cervix is removed no cancer can grow in it as a re-occurrence.

"3. Certain cancers of the cervix are radiation-resistant.

"4. From the work of Bonney and Taussig it has been proved that about 20 per cent of patients with lymph gland involvement can be salvaged by surgery."

Those who advocate this method restrict its use to good operative risks in whom the growth involves not more than the entire cervix and



the upper portion of the vagina. It is not applicable to those cases in which the parametrium is invaded.

Meigs has performed this exacting procedure 100 times without an operative death, and he has had more than forty consecutive cases without development of a single urinary fistula. Of the thirty-six patients who had been operated upon more than three years previously, he reported in 1946 that 77.7 per cent were living and well. Since the many advances in modern surgical technic, especially liberal use of blood transfusion and the antibiotics, have decreased the hazards of this formidable operation, it is hoped that qualified individuals will continue the surgical approach to this problem until time will permit a proper evaluation of its results. At the present time the results of surgical treatment are not significantly better than those following radiation therapy in cases of similar extent. There is little doubt that the general adoption of the radical operation would result in needless mortality and morbidity. Most of us who treat cervical carcinoma should not abandon radiation therapy, rather, we should be quite sure that each patient promptly receives optimal therapy.

### SUMMARY

Whether early cancer of the cervix is treated by irradiation or by adequate surgery it is curable in approximately three fourths of the cases. Practically none of the late cases can be salvaged. Unfortunately at the present time more than 75 per cent of patients apply for definitive treatment after the disease has advanced beyond any reasonable hope for cure. Our duty as doctors is clearly defined in our obligation to educate the public concerning the significance of abnormal bleeding and the necessity of frequent periodic pelvic examination of all women. Medical students, interns, residents and practicing physicians must be made more conscious of these specific duties if we are to accomplish any real progress with our present admittedly deficient methods of treatment.

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# THE DESIRABLE MANAGEMENT OF FUNDAL CARCINOMA

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THE desirable management of any malignant lesion is its elimination in such a way that recurrence is unlikely and the patient's survival assured. This is a difficult goal to attain in many instances for reasons familiar to most of us. Speaking specifically, however, carcinoma of the uterine fundus (or corpus) begins primarily as a localized endometrial growth, with few exceptions tends to spread comparatively slowly, and gives ample warning of its presence in the meantime. This fortunate association of events makes fundal carcinoma much more adaptable to complete eradication than is the case with malignancy in more remote areas of the body. Likewise, a cancer of similar extent in the cervix, certainly an accessible site, has much less chance of eradication since parametrial and lymphatic extension in this region can and does occur much more promptly than in the fundal lesion because of anatomical variations.

The purpose of this clinical presentation is to discuss some factors relating to the etiology, pathology, symptomatology, and diagnosis of fundal cancer which have a distinct bearing upon management, selective treatment, and results.

## ETIOLOGICAL CONSIDERATIONS

Within recent years numerous writers have given earnest thought to the possible influence of unrestrained estrogenic activity on the direct development of endometrial carcinoma. This is perhaps a logical sequence to the earlier postulation that endometrial hyperplasia, although initiated by persistence and excess of estrin, might itself be the precursor of fundal cancer. For anyone particularly interested in this earlier viewpoint, reference to Howard C. Taylor, Jr.'s<sup>1</sup> contribution of 1932 is recommended for initial study or for re-reading. Although Taylor left the final answer unsettled, collective evidence is presented

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in this careful review of his own and earlier work that can well be weighed by any investigator today in pursuing this fascinating subject.

Novak and Yui in 1936,<sup>2</sup> following an hypothesis similar to that of Taylor, were particularly concerned about atypical hyperplasia in the postmenopausal patient, and its association with adenocarcinoma, declaring their belief in a definite carcinogenic relationship between these associated lesions, presumably activated by persistent hormonal stimulation of the endometrium not necessarily from an ovarian source. Their reasoning was disputed by TeLinde in his discussion of the presentation, and he based his disagreement primarily on "what constitutes the minimum histologic changes necessary to a diagnosis of hyperplasia." TeLinde further questioned Novak and Yui's conclusions on the basis of his own experience in finding a similar histologic picture with respect to hyperplasia in postmenopausal endometria, in the absence of adenocarcinoma. A year later Payne's<sup>3</sup> study revealed 2.4 per cent of associated fundal cancer occurring in 534 cases of endometrial hyperplasia (496 premenopausal and thirty-eight postmenopausal). He emphasized further that since carcinoma was five times as frequent in the postmenopausal cases as in the premenopausal ones, then the incidence of malignancy should be higher if hyperplasia is a forerunner of cancer, even though postmenopausal fundal cancer is seen far more frequently than premenopausal, regardless of the endometrial pattern.

Jones and Brewer<sup>4</sup> were not able to demonstrate excessive or unopposed estrogenic action in corpus carcinoma in a group study of sixty-eight such cases based on histologic and anatomic evidence of ovarian and endometrial function. It remained for Fahlund and Broders,<sup>5</sup> in a recent comparative study of postmenopausal adenocarcinomatous and nonadenocarcinomatous uteri, to likewise present an antagonistic viewpoint to the hyperplasia-adenocarcinoma concept by their concluding observation that atrophic endometrium was actually encountered more frequently in malignant than nonmalignant uteri, and that the uninvolved endometrial areas in the group of patients with cancer did not differ materially from those having nonmalignant uteri. The contribution of Fahlund and Broders is especially valuable, too, because of the meticulous review of the literature that it embraces. In this respect, a perusal of Novak and Richardson, Jr.'s<sup>6</sup> study of the proliferative changes in the senile endometrium may well be reviewed with profit, for they show that the long-time concept of the atrophic senile endometrium is not borne out by their finding of 30 per cent of moderate to active stages of proliferation and hyperplasia in a study of 137 cases.

It can readily be seen from this synopsis that there is no indisputable

proof that endometrial hyperplasia, *per se*, is the precursor of adenocarcinoma of the fundus. On the other hand, every worker in the field has probably seen instances in which clinical observation has given the factual impression that hyperplasia has preceded adenocarcinoma, or has observed an area of hyperplasia accompanying frank cancer of the corpus. The evidence to date perhaps represents no more than a histologic coincidence. Still it cannot be denied that microscopic gradations between extreme hyperplasia and adenoma malignum may be such that interpretation with respect to therapy must be decided on the clinical aspect of the individual case in such instances.

In 1942, the senior author and Dr. Jacob Hoffman<sup>7</sup> called attention to the possible use of the term "carcinoid hyperplasia" to describe atypical endometrial hyperplasia, so marked as to resemble closely the histologic low grade lesion generally referred to as adenoma malignum (Grade I). Novak and Rutledge<sup>8</sup> in 1947, in discussing the problem of atypical endometrial hyperplasia simulating adenocarcinoma, presented a similar conception in greater detail. The pathologist bears a heavy responsibility when he announces his decision; the clinician must assume his responsibility just as seriously, for the life of the patient, in the final analysis, is actually in his hands.

It is not strange, then, that today our thoughts have turned more and more toward concepts based upon the investigation of those basic substances that enter into the realm of carcinogenesis by their growth-stimulating properties, particularly with respect to the female sex organs as exemplified by estrogenic activity. The knowledge gained from animal experimentation in the production of malignant lesions by protracted estrin injections has demonstrated their carcinogenic activity when tissue susceptibility has yielded to huge dosage. While Gardner, Allen, Smith and Strong<sup>9</sup> succeeded in demonstrating cervical cancer experimentally in mice through continued estrogenic therapy, Burrows<sup>10</sup> has called attention to spontaneous uterine cancer in rabbits, the occurrence of which suggested the presence of a singular endocrinopathy in these particular animals. Greene<sup>11</sup> states in his report that the incidence of uterine adenomas closely paralleled that of toxemia of pregnancy in rabbits, and infers that the association results from the inability of the damaged liver to inactivate estrin which thereby reaches a carcinogenic level in the blood.

It is quite natural that these phenomena should arouse interest in parallel manifestations in the human, and recent investigative work by Corscaden and Gusberg<sup>12</sup> has been nicely crystallized in a subsequent clinical and histologic survey that has furnished interesting data in four categories made up of his own work and the findings of others. The latter publication by Gusberg, later in 1947,<sup>13</sup> is certainly worthy

of quotation. He first calls attention to the "response of the human endometrium to granulosa cell tumor of the ovary." This association, of course, has been widely reported from various clinics. In our own clinic at Jefferson we have not only observed endometrial cancer with granulosa cell tumors, but have reported two rare instances of granulosa cell tumors occurring in patients with cervical carcinoma and appearing ten years after the arrest of the latter by irradiation.<sup>14</sup> The coincidental finding of hyperplasia with theca cells tumors is equally well-known. Certainly this speaks for an endocrine-tumor relationship. Gusberg then mentions "hyperplasia of the human endometrium following prolonged estrogen administration," and here again we observe a widely-seen clinical feature, whether synthetic or natural estrogens are the activating agents. "Adenocarcinoma of the human endometrium following prolonged estrogen administration" is Gusberg's next category. That such therapy has actually been productive of fundal cancer is certainly controversial, but the occurrence is strongly to be suspected in the reported instances quoted from his own experience and from that of others. We have seen one such possible instance in the Jefferson clinic. Finally, the author refers to the "relation of hyperplasia of the endometrium to the development of corpus carcinoma," the controversial association already commented upon in this presentation. Gusberg approaches this theme from the "endocrine background of patients with corpus carcinoma," as evidenced by physiologic eccentricities. He also refers to their previously published observation that three and one-half times as many women who had received irradiation therapy for menopausal bleeding developed corpus carcinoma than would ordinarily have occurred in the general population. This would indicate that a relatively frequent occurrence of hyperplasia in the menopausal era might well predispose those individuals to endometrial cancer. The implication here is that unopposed endogenous estrogenic stimulation is the initiating carcinogenic factor. It can readily be appreciated that today's postulations are a far cry from the earlier beliefs that fundal cancer was initiated by imperfect drainage from the uterine cavity, either because of cervical stenosis, or because of irregularities due to associated myomas, or that the latter per se were the stimulating factor. However, the high incidence of associated myomas with endometrial cancer may after all merely reflect the influence of estrogenic stimulation and thus "tie in" with more recent concepts.

#### CLINICAL MANIFESTATIONS

We believe that the consideration just given to the possible etiologic factors concerned with fundal carcinoma should be given due weight

when the means of controlling the condition are discussed. Proper management is not merely a mechanical procedure; keen evaluation of the patient as an individual problem, and not merely as a "case," is properly a helpful prerequisite, especially in view of the controversial points that exist with respect to etiology. Of equal importance is a thorough estimation of the clinical manifestations of the disease. In this phase there is much less disagreement than in the former; for here are things we can see and study by physical means, rather than by postulations.

**Physical Peculiarities—The "Cancer Type."**—We have seen various interesting peculiarities among 200 or more patients with fundal carcinoma treated in the Jefferson Clinic during the past twenty-seven years. These findings parallel in many respects the observations of others, notably those of Corsecaden and Gusberg, Randall<sup>15</sup> and Moss.<sup>16</sup> First of all, there is a preponderance of obese or relatively obese women; the rather high incidence of hypertensives, usually with varying degrees of arterial and renal change; the more than occasional diabetic—and, strikingly, an absence of anemia in the vast majority. Postmenopausal bleeding in these women has, in a goodly proportion of them, been due to endometrial carcinoma. A distinctly leukorrhical type of discharge is of much less significance. Naturally, they fall into the group whose average age is 59 years and who comprise nearly 80 per cent of our total fundal cases, since four out of five patients with fundal cancer are over 50 years of age. Roughly a third of them have never been pregnant, and of these about one-half have never married. Also, women with fundal cancer are more likely to have had menorrhagia in the premenopausal and menopausal epochs. Definite postmenopausal bleeding has occurred anywhere from one to twenty-six years after cessation of menses.

From these observations one can almost "spot" the patient who is more than likely to have cancer of the corpus—and thus prepare for her proper management. Certainly all of them should be subjected to curettage, even though vaginal cytologic smears are reported negative. Doubtful or positive smears, while suggestive, must be confirmed by careful curettage.<sup>17</sup> Use of the aspiration technic should be discouraged when attempting to prove or eliminate cancer by curettage; the entire surface of the endometrial cavity should be scraped. While postmenopausal bleeding may be due to polypi, senile vaginitis, cardiovascular disease, or even to fibroids, the odds are against such diagnoses in the patient who presents the distinctive characteristics just mentioned.

**The Premenopausal Patients.**—What about the clinical picture in that 20 per cent of women who are found to have fundal cancer prior to the cessation of menses? In this group the age limit is roughly 40 to



50, although occasionally patients in this category may be under 40. Unfortunately it is among such women particularly that delay in diagnosis and mistakes in therapy can happen, and for good reason. Menstrual irregularities of any type, more likely in this decade, are too often regarded primarily by the patient as a not unexpected feature of "change of life." Hence, the disturbance is given little thought unless the bleeding is either too profuse, uncomfortably annoying, or merely inconvenient. So medical advice is not sought promptly enough. On the other hand, it is not too uncommon for a fear of learning the truth, or an undue sense of modesty, to contribute to this delinquency. Fortunately, both of these possibilities are perhaps diminishing in the light of today's far-flung propaganda for early cancer diagnosis and care.

Granting that a certain proportion of the delay period incident to prompt recognition and treatment results from the ignorance or indifference of the woman herself, it is only too true that the physician first consulted is often the one responsible. He may be too busy to properly examine his patient or be reluctant to do so "when she is bleeding." Many and many a writer and lecturer has called attention to the injudicious and indiscriminate use of endocrine therapy used to "control" bleeding at this time of life.<sup>13</sup> In so doing even the most cursory pelvic examination may be omitted; not only may the helpful diagnostic symptoms be masked thereby, but the loss of time occasioned makes less the chance of recovery if and when the true state of affairs finally becomes apparent.

Another hazard is that of a diagnostic error. Fibroids may be discovered, for instance. The abnormal bleeding is attributed to this common uterine tumor, inadequate surgery may be carried out, and an accompanying cancer found, not by the surgeon, but by the pathologist in the partially resected uterus. Similarly, irradiation therapy with x-ray may be employed to control the hemorrhage and thus coincidental cancer may be overlooked. In both such instances, tragedy might well have been averted by the cancer-conscious practitioner who would first have carried out diagnostic curettage to discover or rule out that possible adenocarcinoma of the endometrium lurking close by the fibroid growth. Many of us too, have seen a conspicuous but benign cervical polyp removed as the source of abnormal bleeding, while the carcinoma within rests undisturbed because of failure to curet the uterine cavity at the same time that the polyp is removed.

These errors of omission and commission are really too frequent. Constant vigilance must be exercised—first, by the family doctor in evaluating the cancer potential of abnormal premenopausal bleeding, and second by the surgeon alert to the possibility that fundal cancer

may accompany an obviously benign uterine lesion—if correct diagnosis and appropriate treatment are to be attained.

### DIAGNOSIS AND TREATMENT

It is our feeling that diagnosis and treatment are so closely associated that the discussion of one complements the other. What has been said of the clinical manifestations correlates to a degree the remarks regarding the clinical considerations; without repetition it can be seen that both are truly allied with diagnosis and treatment in the broader sense.

**Variations in the Histologic Picture.**—To begin with, it is essential to recall that there is considerable variation in the histologic picture presented by fundal carcinoma. It is probably true that the majority of the lesions fall into the panel of a low-grade type of malignancy—papillary adenoma malignum (Grade I) and adenoma malignum (Grade II). A lesser proportion represent an intermediate grouping—adenocarcinoma (Grade III), while solid cellular, or diffuse anaplastic adenocarcinoma (Grade IV) is the least common, being a very high grade malignant lesion. Adenoacanthoma is the rarest. These histologic facts are of considerable importance when diagnosis and treatment are considered. As far as diagnosis goes there is little difference in symptomatology with respect to the gradation of the tumor. In regard to treatment, on the other hand, certain observations have been made in which the histologic picture plays a distinct part. It should also be recalled, from what has been said before, that gradation is not always as simple a matter as it would appear on paper. Because of this difficulty we have tried to simplify this phase of the problem in the Jefferson Clinic and Laboratory by confining our classification to low, intermediate and high grades of malignancy, and this interpretation has proved popular in other clinics as well from the viewpoint of microscopic diagnosis.

**Clinical Classification.**—The clinical grouping of fundal cancer is by no means standardized, and various plans are in vogue in different clinics. These have been discussed and compared in a previous presentation by Scheffey, Thudium and Farrell.<sup>19</sup> The classifications that are extant vary in character from those based simply upon operability and nonoperability, and upon the gross extent of the disease as interpreted by the examiner, to the comparative size of the uterus when palpated, with or without apparent extension beyond it. In the Jefferson Clinic we have consistently followed the grouping of the American College of Surgeons. At present the Editorial Committee of the "Annual Reports on the Results of Radiotherapy in Cancer of the

Uterine Cervix," as formerly published by the Health Organization of the League of Nations, is engaged in preparing a possible grouping relating to cancer of the corpus, similar in scope to that of the League of Nations classification of cervical cancer. This work will in all probability be carried on under the aegis of the World Health Organization of the United Nations in Geneva. While a standardized classification of the clinical extent of the disease would be most acceptable to all concerned, it seems to us that its chief importance will be in the field of comparative statistical study and that further discussion of this purely academic phase is not too pertinent to this presentation. What we are concerned with at this time is the desirable management of fundal cancer in its various phases as the clinician sees it.

**Surgical Eradication.**—We have more or less summarized the symptomatology of fundal cancer, the age incidence, and the conditions under which its presence may be suspected with reasonable assurance of confirmation. Traditionally, the diagnosis and treatment of fundal carcinoma was largely empirical and similar, in general approach at least, to the management of cervical carcinoma. From the pioneer abdominal hysterectomy of Freund in 1878, from the later techniques of Werder and Wertheim, together with the technical refinements of Ries and Clark, we have come a long way to the present-day masterly procedures of Bonney, the late Frank Lynch and of Joe V. Meigs.

The radical operation for cervical cancer, to be successful, depends upon complete removal of all regional lymph nodes, if and when this procedure is indicated. This has not held true for cancer of the corpus. Before the wider implications of total hysterectomy were appreciated, the supravaginal technic was for years the procedure of choice in patients with benign disease involving the fundus, and many times in the past fundal cancer was treated in like fashion with inevitable recurrence only too often. With the newer concept of diagnostic curettage, it became evident that cancer of the endometrium could be discovered before carrying out a major procedure, and thus departure was soon to be associated with the development of total hysterectomy and adnexal removal for proven cases of fundal cancer. Naturally a certain proportion of the patients so treated harbored cancer that had invaded the uterus deeply, or had even extended beyond it without clinical evidence of the fact. In such instances recurrence was often relatively prompt. In other patients local pelvic extension or even more distant metastases were apparent and surgery was either purely palliative or merely an "open and close" proposition. Nevertheless,

and especially in the presence of low grade lesions, permanent survival for a long period of time occurred after adequate surgery.

The same fortunate result holds true today, but it cannot be denied that in some instances such recoveries might possibly be the result of a mistaken histologic diagnosis, whereby a bizarre endometrial hyperplasia had or has been labeled carcinoma. Occasionally cases of extensive pelvic carcinomatosis have been and are encountered in which involvement is present in both the ovary (or ovaries) and in the uterus, making it difficult indeed to decide which site is the primary one. In any event, and especially where intermediate and high grade degrees of malignancy are encountered in the removed uterus and/or in the adnexa as well, postoperative recurrence or general metastases has unhappily been only a question of a few months, even though surgical eradication was believed to have been effected at the time of operation.

**Irradiation Therapy Alone or Combined with Surgery.**—With the advent of radium and x-ray, and with the spectacular results obtained by their use in the field of cervical cancer, it was only natural that the clinician should turn to these alleviative and curative forces. Not only did irradiation come to be utilized almost exclusively in aged or debilitated individuals, and in those handicapped by obesity, diabetes, cardiovascular and renal disease, but also to some extent in so-called good risk patients. Many times the results were striking either because of the radiosensitive lesions that these women harbored, or because the growth was small or well localized and readily accessible to the source of the irradiation. Before long, however, it became apparent that only arrest of the disease occurred in a proportion of these people, for symptoms returned at varying intervals thereafter. Naturally, this has led more and more to the realization that irradiation has a limited value with respect to permanent cure and that surgery has a major role to play in the final eradication of fundal cancer whenever it can be utilized in a suitable capacity.

The next step in therapy was a logical one. Why, if irradiation had proved reasonably effective in a certain proportion of patients with fundal cancer, and if surgery too had proved effective in another group, could not these two therapeutic measures be combined in some way to complement each other whenever possible? Just that has happened and the literature is now abundant with reports of experience and accomplishment with the preliminary use of irradiation as a precursor to surgery in the management of fundal carcinoma. The summation of these clinical findings has resulted in the establishment of the

rational procedures now prevalent in most gynecologic clinics today.

While differences of opinion exist with respect to whether radium or x-ray is superior in the part that preliminary irradiation plays and just how these factors should be employed, the facts remain that, when suitably used, irradiation seems to be responsible for certain accomplishments than stand out in the experience of many of us. Irradiation tends to promote local devitalization and attenuation, if not complete destruction of the growth, reduction of infection and sealing of lymphatics, thus lessening the possibility of cancerous dissemination when surgery is employed later on, and finally reduction of the incidence of recurrent growth in the vaginal vault scar. These are important clinical observations, but it should be stated emphatically that when irradiation is used prior to surgery, it is not used with the expectation of eliminating the lesion *per se*, but for the reasons just stated. The reports in the literature show that in removed uteri, residual disease is apparent in 50 per cent and more of them. Invasive myometrial growths remain unscathed as a rule.

One of the best and most recent contributions dealing with a careful microscopic study of previously irradiated uteri surgically removed for corpus carcinoma is that of Stowe.<sup>20</sup> His conclusions coincide with our concept of the positive limitations of irradiation therapy unless its use is considered in the light of subsequent surgery whenever possible. On the other hand, it is recognized that, in the case of some patients in whom surgery cannot play a part because of unalterable contraindications, irradiation has to be relied upon. It is in such cases that the constant improvements being noted in methods of irradiation, especially with radium, may rightly increase our optimism. In this respect numerous innovations in the technique of the intrauterine application of radium have been introduced from time to time. Outstanding early workers in this field were the late Curtis Burnam and Heyman of Stockholm, and others too have contributed to this technique. In recent years ingenious applicators have been designed by Schmitz and Schmitz,<sup>21</sup> Friedman,<sup>22</sup> Nolan and Arneson,<sup>23</sup> Crossen<sup>24</sup> and Stowe. For detailed descriptions the reader is referred to the various authors' descriptions in their original publications.

#### BRIEF SURVEY OF REPORTED RESULTS OF TREATMENT

Prior to the advent of combined radiologic and surgical treatment, over-all results were reported primarily in two categories—surgery and irradiation. A typical picture of such results is shown in Arneson's<sup>25</sup> collected statistics involving 1935 patients treated either surgically

or with irradiation. In the former group the five-year survival amounted to 57 per cent; in the latter to 37 per cent. Other individual reports in the literature vary but little from these figures—some relatively higher, and some lower.

When we consider those reports in which treatment has been with combined irradiation and surgery, misconceptions result. This is because there has been considerable variation in the type of irradiation used and in its precedence or sequence with respect to surgery; also with respect as to whether or not the latter was adequate, inadequate, or only palliative from the technical viewpoint. Where, however, a planned technic of therapy has been recorded in a separate division, recent reports are decidedly encouraging.

Thus Corseaden, in 1944,<sup>26</sup> presented a five-year survival figure of 72 per cent, and with his own remarkable rate quoted those of others who had employed intrauterine radium prior to hysterectomy. These quotations range from Healy and Brown's 55 per cent figure in one series, to Heyman's 78 per cent in a series of sixty-five patients and to Arneson's 90 per cent in a group of ten patients. Very recently Arneson and his co-workers<sup>27</sup> have announced that their best results have been with multiple sources of radium in the uterus followed by hysterectomy, to the extent of 79 per cent of five-year survivals as compared with 54 per cent where a tandem application was used. They also add the observation that in removed, irradiated uteri that showed no evidence of residual tumor, the survival rate amounted to 88 per cent. (They explain an 84 per cent survival among eighteen patients treated solely with surgery "on the basis of favorable clinical material.")

Miller and Henderson,<sup>28</sup> the leading exponents of preoperative x-ray prior to surgery, reported a five-year survival rate of 77 per cent in 1946, although in a smaller group of patients in whom radium was employed instead of x-ray, the result was 86.6 per cent, and the ten-year survivors in this group amounted to 81.8 per cent as compared with 65 per cent of ten-year survivors in those patients having preliminary x-ray. With regard to intrauterine radium applications, the general impression is that larger dosage yields superior results, although Gray, Friedman and Randall<sup>29</sup> reported that unusually large doses applied in the case of seven of their patients had not eliminated the local growth in six of them when the removed uteri were studied microscopically. It is the consensus as previously stated, however, that surgery should always be resorted to whenever possible after preliminary irradiation has been utilized. An increased latitude for

surgical procedures has been notably enhanced with the modern methods at our disposal, such as intravenous therapy, blood transfusion, antibiotic medication and improved anaesthesia

### MANAGEMENT AND TREATMENT IN THE JEFFERSON CLINIC

We have devoted considerable discussion to the general question of diagnosis, management, treatment and results as viewed by our colleagues elsewhere. Obviously, it has been impossible to quote at length the experiences of all those mentioned. Furthermore we could not, in the space allotted to us, refer to the splendid and painstaking efforts of others with whose work we are so familiar, and we apologize for any such omissions. We shall present concisely and by illustration the methods that are favored in the Jefferson Clinic and to speak in addition of the results that we have been fortunate enough to attain in the treatment of fundal carcinoma.

It is our firm belief that a searching history and meticulous evaluation of the woman with abnormal premenopausal and menopausal bleeding, and of the individual with definite postmenopausal bleeding will disclose sufficient data to make a tentative diagnosis of uterine cancer. With the cervix and cervical canal eliminated as a probable site of malignancy, attention is focused on the body of the uterus and the adnexa. The obvious presence of senile vaginitis, polypi or adnexal enlargements does not divert our attention from the presence of possible endometrial cancer. Vaginal smears are studied for cytologic evidence of abnormal cells (Papanicolaou technic). A negative report is not accepted as a deterrent to further diagnostic study, but a doubtful or suspicious report is given due credence.

The next step depends upon the size and contour of the uterus as estimated by bimanual examination, and by the absence or presence of adnexal enlargements. At the same time the physical habitus of the patient, and her potentialities as a candidate for possible surgery are considered with the usual care that should be exercised in this regard.

If the uterus is regular in outline, mobile, either relatively small or moderately enlarged, and no adnexal abnormalities can be detected, we proceed on the assumption that a thorough curettage will rule out carcinoma or disclose benign abnormalities. At the same time various sources of radium are available for intrauterine application. Most commonly we use two or three capsules of 50 mg. each screened with 1.5 mm. of platinum and of 2.5 cm. "active length" with a diameter of 1.5 mm. Figure 396 shows diagrammatically how these capsules are arranged in tandem and encased in paraffin tubing. Whether two or three units are employed depends upon the length and contour of

the uterine cavity as evidenced by sounding and curettage. There being no physical contraindication to the proper placement of the tandem, the curettings, placed in formol-alcohol solution, are sent at once to the laboratory for immediate preparation of a paraffin section which is available for study in four hours. If a malignant condition is present the radium is allowed to remain for a total dosage of approximately 5000 mg. hr. If the tumor is benign, it is removed at a time compatible with a dosage suitable for control of the abnormal bleeding. If endometrial cancer is present, total hysterectomy and bilateral salpingo-oophorectomy follows in six to ten weeks, dependent upon the radium reaction and all related factors. This procedure is spoken of

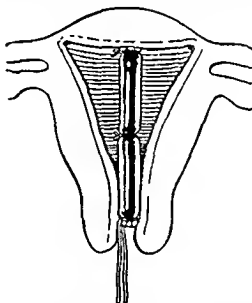


Fig. 396—Diagrammatic representation of the straight intrauterine tandem by which two or more radium capsules can be utilized for placement in the endometrial cavity pending the result of the rapid histologic report of the curettings

as the "planned technic." No postoperative x-ray is employed unless there is gross evidence at operation of extension beyond the uterus, or of metastases. In our experience the tandem application permits of the management just described, and for the reasons stated, to better advantage than would be possible with the application of multiple units packed within the uterine cavity as advocated by Arneson. The advantages of this plan, which Heymann<sup>30</sup> has utilized for so long a period, will be mentioned later in another connection. The inadequacy of even large dosage with the hysterostat technic has already been emphasized in our quotation from the experience of Gray, Friedman and Randall.



Naturally, deviations from a planned technique occur. Not all the patients appearing for treatment can be managed in the above fashion. In those having obvious extension of disease beyond the corpus, diagnostic curettage confirming the diagnosis would be followed by external irradiation with x-ray, as well as with an intrauterine application of radium.

When examination in the operating room at the time of initial curettage and proposed radium application reveals a uterine cavity too tortuous or too distorted by concomitant myomas or polypi to permit of primary intrauterine irradiation, either one of two things may be done. First, if the curettings are minimal or moderate, surgery may be carried out forthwith, its extent to be determined by examination of a frozen section of the curettings while the operation is proceeded with. The latter is only of help if the pathologist can state unequivocally that cancer is present, with respect to frozen section curettings this is often impossible to do. Second, if the curettings are abundant and grossly suspicious, we may stop with curettage, doing no more than that under the circumstances until receiving the pathologist's routine report on a permanent section in twenty-four to thirty-six hours. The disadvantage here is that if the curettings are benign, surgery cannot be undertaken with safety for a matter of several weeks, in our opinion. If they are malignant, then x-ray treatment is depended upon as the preliminary step in therapy. If in addition to the above circumstances, adnexal disease is found, and particularly if it is suggestive of an ovarian or tubal mass or neoplasm, an immediate and radical surgical approach is probably the best procedure, with a frozen study of the curettings being made in the meantime for whatever information this purely tentative study may yield.

**Management of the Poor Risk Patient.**—A discussion of our management of the poor-risk patient is now in order. Rehearsing the criteria that govern such a classification is not necessary here, for they have already been narrated. Irradiation is primarily thought of in this group, either with radium alone, or in combination with x-ray. To our way of thinking, it is here that the most complete application of radium sources must be worked out by intrauterine methods, if this is not possible, then external irradiation with x-ray is our resort. Much of course depends upon the size of the uterus and the extent to which the endometrial cavity is available for participation. The possibility of damage by instrumental perforation of the uterus is enhanced in these individuals, too, so that more than usual care and gentleness must be exerted in carrying out the method of application decided upon. In the smaller uteri, tandem applications are simplest and safest.

In larger cavities there is a place for the hystero-stat (although we have not used it) but particularly for thorough packing with multiple small capsules of radium. There is no doubt that these small units, relatively weak in radium content, distribute their activity to superior advantage, even in a somewhat irregular uterine cavity. Sampson<sup>21</sup> long ago pointed out conclusively the disadvantages of tandem applicators in uterine cavities of such a type. Although practically all of the intra-uterine irradiation to date in the Jefferson Clinic has been with tandem applications, we are convinced of the desirability of, and have embarked upon, the *multiple source technic* for use when the individual conditions that have just been commented upon exist. This is said with

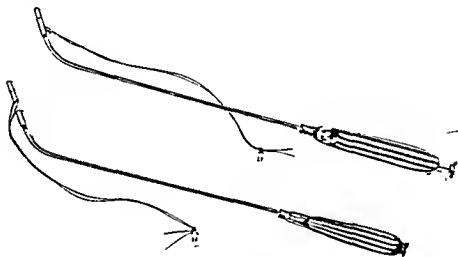


Fig 397 —The upper picture shows a capsule, tagged with a numbered thread, fitted into the introducer mentioned in the text. Note that the plunger of the instrument is out. The lower picture represents the mode of extrusion when the plunger is pressed in.

due regard for the fact that the end results noted in the conclusion of this presentation have been achieved with the older and more commonplace method.

Figure 397 illustrates the applicator used in the Jefferson Clinic for the introduction of small radium units into the uterine cavity. It was designed by Dr Theodore P. Eberhard, Assistant Radiologist to the Jefferson Hospital and Assistant Professor of Radiology in Jefferson Medical College. Eberhard has merely modified the introducer originally devised by Nolan and Arneson as mentioned previously. Capsules containing any desired unit of radium can thus be introduced serially until all available space in the uterine cavity is exhausted.

To each capsule is attached a numerically tagged heavy thread, so that each can be removed in reverse order from its introduction. Figure 398 demonstrates by roentgenogram the presence of fifteen 10 mgm capsules in position in the uterine cavity of a cancer patient. In this instance each capsule with an active length of 10 mm, a diameter of 4 mm, and a screening of 0.9 mm of platinum, contains two cells, each containing 5 mg of radium. A total of five such cells can be accommodated in the capsule if desired. The latter in turn are each screened with 0.1 mm. of platinum, thus increasing the total screening



Fig. 398.—Roentgenogram showing fifteen 10 mg radium capsules packed into the uterine cavity with the introducer. The number and relatively small size of the units permit them to be distributed within the contours of the uterine cavity.

employed to 1 mm. By the use of this radiologic armamentarium, local conditions can be met nicely and appropriate dosage calculated.

We are coming to realize more and more, however, that even the substandard risk patient may eventually warrant surgery either because of revised judgment or as a result of necessity. A case in point in our Clinic well illustrates this contingency.

Mrs. D. F. was operated upon elsewhere in 1940 when curettage, trachelorrhaphy, anterior and posterior colporrhaphy, uterine suspension, and appendectomy were performed. No curettings were obtained, although "spotting" was complained of at the time. In March 1942 vaginal bleeding occurred, as-

cribed to high blood pressure, and stilbestrol was administered over a period of several months because of vasomotor symptoms.

The patient was referred to the senior author in December and curettage was carried out with a tandem of 100 mg. of radium *in situ* pending a rapid report. At the same time anterior and posterior colporrhaphy were repeated because of recurrent lesions. Adenocarcinoma, intermediate grade, was reported and the radium was allowed to remain *in situ* for a total dosage of 4800 mg. hr. The patient was 61 years of age, and because of obesity, hypertension and paralysis agitans, it was decided not to carry out subsequent surgery.

All went well for nearly five years. The uterus remained small and mobile, but occlusion of the cervix had been noted as early as four or five months after operation. There was a lapse in follow-up visits between the fall of 1945 and the fall of 1947. During this time the patient reported by telephone that she had no pelvic disturbance, but did volunteer the information that she was being treated for "nerves" by another physician. During the spring and summer of 1947, the same physician treated her for "fermentation of the bowels" which he said was causing recurrent attacks of abdominal pain that were becoming progressively worse.

The patient finally returned to the senior author in September 1947 for consultation. There had been no uterine bleeding. Examination revealed a tender abdomen, an occluded cervix and a markedly enlarged and sensitive corpus, suggesting hematometra or pyometra, very probably associated with recurrent or unarrested carcinoma. Her general condition was, of course, no better, but admission to Jefferson Hospital was arranged, a thorough clinical survey made, and operation decided upon as a necessity because of the abnormal condition of the uterus and partial intestinal obstruction due to extrinsic bowel factors.

Operation took place on September 27, 1947. Cervical dilatation was decided against and wisely; only vaginal antiseptics was carried out. Abdominal section revealed dense adhesions at the site of the initial uterine suspension, involving the parietal peritoneum and the large and small bowel extensively. Bilateral chronic salpingitis and peri-oophoritis were noted in addition to an enlarged and somewhat softened uterus. Although technically difficult, total hysterectomy and bilateral salpingo-oophorectomy were performed satisfactorily. There was no gross evidence of malignant extension outside the uterus. The most pronounced annoyance was encountered in closing the peritoneum. Convalescence was unusually satisfactory, and the patient has remained well to date.

Figure 399 depicts the meised removed uterus, with a partial view of the adherent left adnexa. Predominant was the large amount of soft tumor mass showing diffuse necrosis. Remarkably, no invasion of the myometrium was demonstrable. There was no microscopic evidence of extension or metastases to the tubes or ovaries. The serosanguinous fluid present could not escape vaginally because of the occluded cervical canal, hence, the absence of bleeding and discharge.

The lesson presented by this patient's experience is two-fold. first, the continued tumor growth over a period of nearly five years without

invasion of the myometrium or recognizable metastases, second, the realization that obligatory surgery can be borne by the poor-risk patient in the light of today's technics. This patient's course has been a tremendous spur to us in our conclusion that eventual removal of the irradiated uterus should always be our goal. A similar case is recorded in our series—a patient, treated solely with radium twelve years ago at the age of 61, developed in 1943 a situation like that described, underwent complete pelvic surgery uneventfully, and is now well and free of disease at the age of 73.



Fig. 399.—Removed uterus of a patient (D. F.) showing extensive residual or recurrent adenocarcinoma present when total hysterectomy and adnexal removal were carried out four years after radium therapy was administered (case described in text.)

#### SUMMARY OF RESULTS OBTAINED IN THE JEFFERSON CLINIC

The most recent complete report of the treatment of fundal carcinoma in the Jefferson Clinic was reported in 1946.<sup>37</sup> Space in this presentation will not permit of so complete a review, which will appear later at an appropriate time. Our present endeavor is to bring that report up to date only in certain aspects.

Eligible to date (1921-1948) for five-year survival statistics are 138 patients treated in the Jefferson Clinic (ward and private patients, Division of Gynecology). Of these 77 have lived from five to twenty-three years, or 55.8 per cent. This is the absolute and relative figure,

irrespective of type of treatment, and represents a follow-up of 100 per cent of all patients seen and treated.

**Irradiation Therapy.**—X-ray, radium, or radium and x-ray was employed in sixty-six, of whom thirty-one have survived from five to nineteen years, or 47 per cent. With radium alone, the figure is 51.7 per cent; with radium and x-ray it is 45.7 per cent. Two patients treated only with x-ray did not live very long afterward.

**Surgical.**—Adequate, inadequate or merely exploratory surgical measures with or without the addition of irradiation in some form, or administered without regard to a planned technic, were employed in the case of forty-nine patients of whom twenty-five have survived from five to twenty-three years, or 51 per cent.

**The "Planned Technic".**—Irradiation therapy followed by resection has been used in twenty-three patients, of whom twenty-one have survived from five to sixteen years, or 91.2 per cent. Of the four patients who died of recurrent cancer, two exhibited high grade malignancy (Grade IV). Five of the surviving patients had the same histologic type. Managed in addition by this technic are thirty-six more patients of whom thirty-five have survived from one to four years, one to date having died of recurrence with metastases. Residual carcinoma was reported in 56 per cent of removed uteri but it is conceivable that such areas may have been missed in some. It seems to us that this record speaks for itself and is more than encouraging evidence of the value in our hands of the use of preoperative irradiation exclusively with radium in the treatment of fundal carcinoma. There has been no operative mortality among these 59 patients.

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## THE TREATMENT OF UTERINE FIBROIDS

FRANKLIN L. PAYNE, M.D., F.A.C.S.\*

DISCUSSION of the management of uterine fibroids should be introduced by consideration of certain fundamental truths concerning the life cycle of these tumors. They begin as benign foreign bodies in the uterine wall and their growth is dependent upon stimulation from the ovarian secretion. So long as this stimulation continues they grow with varying rapidity but as soon as the stimulus disappears with the menopause they undergo regression with considerable decrease in size and partial or complete subsidence of whatever symptoms they may have produced. Many fibroid tumors grow to moderate size with no evidence of their existence to regress at the menopause leaving their host oblivious of their existence. When they do cause difficulties the symptoms arise from either associated ovarian and endometrial dysfunction with abnormal bleeding or from the actual physical presence of foreign bodies in the uterus and in the pelvic cavity. Their presence, depending upon their size and position, may cause pressure symptoms such as a sense of weight, vague pelvic pain, or dysfunction of the contiguous pelvic structures. Acute pain rarely occurs except in dysmenorrhea associated with myomas or in the event of a sudden circulatory accident. Chronic or subacute pain follows benign or sarcomatous degeneration of fibroid tumors. The former is common, the latter is rare as evidenced by the fact that only 1 to 2 per cent of the removed tumors show sarcomatous change.

In view of the fact that uterine fibroids may give rise to no symptoms, that they regress following the menopause and that they have a very low potentiality for malignant degeneration, the mere presence of a uterine myoma is no indication for active intervention. The management of such tumors may be divided into four general methods: simple observation, hormone therapy, irradiation and surgical removal. While we may formulate general rules concerning the indications for each of these types of management, the importance of individualization and consideration of extraneous circumstances in each case can not be too strongly emphasized. Either plan of therapy has its particular indications and limitations and there exists no competition between the four plans. A patient who begins under one regimen

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may develop symptoms or signs at any time to place her in one of the other groups

### OBSERVATION

Observation is indicated under the following circumstances

1. In a patient who is approaching the menopause with a fibroid that is giving rise to no symptoms and is no larger than the size of a three months' pregnancy, there being no question as to the certainty of the diagnosis, observation is indicated. Such management is safe because of the expectation that regression of the tumor at the time of the menopause will obviate the necessity for active intervention.

2. In a lesser group careful observation is indicated in the presence of small fibroids in young women who are anxious to have children prior to surgical treatment. In selected cases it is considered wise to defer removal of the tumors until the desired pregnancies have been accomplished since small myomata usually do not interfere with normal pregnancy and childbearing. Should the conception terminate prematurely, however, myomectomy should be done before another pregnancy is undertaken.

3. A third indication for observation is the presence of a symptomless postmenopausal fibroid tumor which is not increasing in size. Should the tumor give rise to discomfort or pain or should it be associated with postmenopausal bleeding immediate operation is indicated. This type of management presupposes a very accurate evaluation of symptoms and unquestionable diagnosis. If there is doubt concerning the diagnosis, examination under anesthesia is indicated and if doubt remains operation is indicated. The patient is instructed to return at regular intervals, usually every six months, for questioning concerning pain, abnormal bleeding, or pressure symptoms and for careful examination. Should indications for more frequent visits arise the interval is decreased. Between visits the patient is to report pain, pressure symptoms or abnormal bleeding, particularly intermenstrual spotting immediately. Estrogen therapy is interdicted because of the probability that it tends to increase uterine bleeding and the possibility that it may interfere with the normal regression of the tumor at the time of the menopause or even stimulate more rapid growth of the tumor in younger women. Patients who are managed by periodic examinations should be informed of their condition and reassured concerning the remote likelihood of malignant changes. They should be warned of the importance of regular visits and of the possibility that active intervention may become necessary at a subsequent date. Approximately 50 per cent of this group will pass through the menopause

with regression of the tumor and no need for further treatment except occasional gynecologic examinations.

### HORMONE THERAPY

As the various endocrinotherapeutic agents have been introduced they have been tried in the management of uterine fibroids. The estrogens are contraindicated and the corpus luteum hormone has no effect. The androgens have desirable effects in carefully selected cases although these results are temporary. This hormone must be administered with the greatest care in order to avoid the untoward reactions that follow heavy dosage. Certainly no more than 300 milligrams per month should be given. Androgen therapy does decrease the bleeding in many instances of menorrhagia associated with small uterine fibroids. The presence of metrorrhagia should always be investigated by means of a diagnostic curettage. Androgens temporarily decrease the size of the uterine fibroid but the original dimensions return soon after it is discontinued. It has been the experience of the author that in patients approaching the menopause with small tumors who have menorrhagia and no other symptoms, the cautious administration of this material often will decrease the blood loss until natural processes render further therapy unnecessary. A similar happy result occurs in the presence of small uterine fibroids in younger women who are anxious to defer operation temporarily. The final position of this therapy has not been determined finally. Thus far, if given under carefully regulated restrictions in instances of menorrhagia only, it seems to be safe and effective as a palliative measure. In the event that neither of the two preceding plans is applicable, active therapy is instituted in the form of either irradiation or surgery. Both of these have specific indications, limitations and contraindications and neither is a competitor of the other.

### IRRADIATION

While the field of usefulness of both radium and x-ray therapy is limited they are fixed as satisfactory and safe measures in the management of certain types of uterine fibroids. A preliminary curettage is indicated in all patients who are to be treated by irradiation, whether intracavitary or external. This is done to eliminate the possibility of pregnancy, a submucous fibroid or polyp, and endocervical cancer and the concomitant existence of an endometrial carcinoma which is known to occur in approximately three per cent of myomatous uteri.

Radium therapy is indicated in two age groups: first, those who are

may develop symptoms or signs at any time to place her in one of the other groups.

### OBSERVATION

Observation is indicated under the following circumstances:

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tion to the blood loss suggests the presence of benign or malignant degeneration for which surgical removal and not irradiation is the only treatment.

In general, x-ray therapy is indicated when active measures are necessary and immediate surgery or the use of radium is contraindicated. It is used as a temporary measure following curettage to control bleeding in the presence of profound anemia associated with fibroid tumors. The bleeding ceases in one to three weeks, the patient's general condition improves and decision concerning surgical removal of the tumor may be made later. Many times in addition to the control of bleeding, the x-ray therapy has resulted in such regression of the tumor that its surgical removal is not necessary. Occasionally certain general conditions such as extreme obesity, cardiovascular or pulmonary disease contraindicate major surgery and at the same time local conditions, as previously enumerated, prohibit the use of radium. Curettage and a sterilizing dose of x-ray therapy is the only answer and usually it proves to be safe and effective. Sometimes local conditions alone may indicate external irradiation, such as large tumors that are irremovable because of multiple postoperative adhesions, extensive residual pelvic inflammation or widespread endometriosis. The regression that follows this treatment reduces the difficulties of subsequent operation and occasionally even eliminates the need for subsequent surgery. While the employment of curettage and an x-ray menopause in myoma therapy is infrequent, 2 to 3 per cent of the cases in our experience, its safety and dependability demand its use in many of the most severely complicated tumor problems that we see.

### SURGICAL TREATMENT

Surgical treatment consisting of either myomectomy or hysterectomy is the proper approach to about three-fourths of the fibroids that require active treatment.

**Myomectomy.**—Myomectomy is applicable in from 10 to 15 per cent of the cases. Its greatest indication occurs in young patients who wish their procreative and menstrual functions preserved. The age limits range between 20 and 40 years. In the treatment of sterility multiple myomectomy should be deferred until all the possible causes of infertility, both male and female, have been eliminated. The size and distribution of tumors for which myomectomy is applicable varies with different authors. While some believe that 25 to 35 per cent of the patients who need treatment for fibroid tumors should be treated by this operation our incidence ranges from 6 to 10 per cent. It is unwise for a surgeon to commit himself to a multiple myomectomy prior to

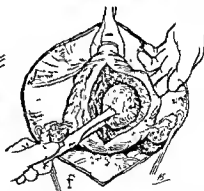
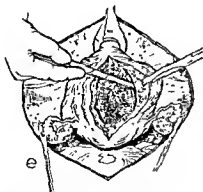
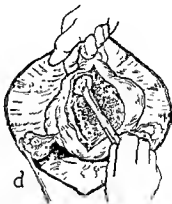
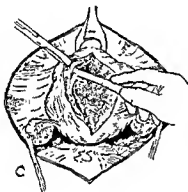
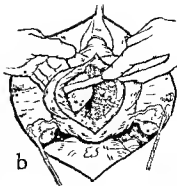
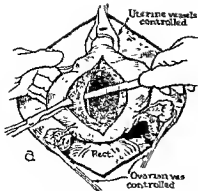


Fig. 400 —Bonney's tunneling operation for the removal of multiple tumors through one primary incision in the peritoneal coat of the uterus

exposure of the uterus for occasionally he may find to his chagrin and to the great disappointment of the patient that a hysterectomy is necessary after commitment to a lesser procedure. Deep intramural and submucous tumors are removable readily but injury to the myometrium and endometrium may be so extensive that the remaining uterus is more dangerous than valuable to the patient.

Myomectomy is attended by more hemorrhage than hysterectomy and preparation should be made to replace the blood immediately. Numerous devices have been suggested to prevent blood loss, such as fingers of the assistant, rubber-covered clamps or a rubber tourniquet around the lower uterine segment. The dangers of venous complications and hematomas following these measures have prevented their general adoption. The local injection of pituitrin or pitocin into the myometrium is of distinct value in reducing the bleeding at the time of operation. Great care must be exercised, however, in controlling all bleeding for there will be a tendency to an increase in the ooze after the reaction to the pitocin has subsided.

Multiple tumors may often be removed through one incision in the visceral peritoneum by tunneling through the myometrium as described by Victor Bonney (Fig. 400). Incisions that are made in the

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the secondary incision a volsellum is attached to it and traction made. Sometimes a straight pull will free the fibroid, but more often twisting movements have to be made to aid the work of the scalpel handle

*c.* An incision is made for a second tumor lying to the left of the midline, further out and more superficial than the first tumor removed. It is also smaller. The volsellum is refixed further down on the left edge of the primary incision and everted. A stabbing cut is made down to the fibroid, which meantime should be held fixed by the fingers of the left hand (not shown). When the fibroid is reached the wound is broadened by the blade after which the handle of the scalpel is introduced and the fibroid is loosened as described previously

*d.* The fibroid is extracted by pushing the volsellum down the length of the secondary incision, opening out and grasping it, pushing at the same time with the fingers of the left hand into the jaws of the instrument. If there is difficulty getting hold, the scalpel handle must be reintroduced and further separation effected until at last a firm grip is obtained. The part played by the left hand is very important. Once the tumor has been secured by the fingers it should on no account be let go until it is removed

*e.* A long secondary incision is made for a large, rather deeply embedded tumor on the other side of the primary incision. The volsellum is attached to the right edge of the primary incision and pulled upon to evert the raw surface. The fibroid is steadied with the fingers (not shown).

*f.* As the incision is large a finger can be inserted to separate the mass of the tumor. A volsellum is introduced through the secondary incision and three forces are brought to bear—the pull of the volsellum, the scoop of the finger and the pressure exerted from outside by the fingers of the left hand. The fibroid soon emerges through the mouth of the secondary incision and with a twisting pull is brought clear away.

(Modified from Bonney, *Myomectomy and Ovarian Hysterectomy*, Paul B. Hoeber, Inc., publishers)

uterus may be covered by advancement of the bladder or omental transplants and the so called "hood operation" suggested by Bonney will place the line of closure on the anterior surface of the uterus (Fig. 401) Multiple myomectomy is known to carry a slightly increased risk over that of hysterectomy. This risk may be reduced to a minimum, however, by meticulous hemostasis and tissue apposition, by replacement of blood and by extreme care in peritonealization. The long-term results of this operation justify its continuation, for subsequent pregnancy occurs in from 25 to 30 per cent of the instances, with a cesarean section incidence of 30 to 35 per cent. Section should be considered after multiple deep myometrial incisions or after a complicated postoperative convalescence. The age of the patient or various obstetric considerations may tip the scale in the favor of cesarean section.

Multiple myomectomy relieves the pain that accompanies menstruation nine out of ten times and it relieves the menorrhagia in approximately 70 per cent of the instances. The term "recurrence of myomas" is a misnomer for they do not recur but other tumors develop that have not been detected at the original operation. The incidence of this development ranges from 2 to 6 per cent according to different authors. Victor Bonney quotes an incidence of 2.3 per cent "recurrences" in 380 cases. The chances of this occurrence are almost nil if the patient is 35 years of age or older. Myomectomies are contraindicated during pregnancy because of the danger of abortion, hemorrhage, hematomas or infection. At the time of cesarean section they are contraindicated for the same reasons except for the removal of subserous pedunculated tumors. While abdominal myomectomy is tedious and slightly more dangerous than hysterectomy, its compensations in terms of future happiness and usefulness more than justify

cervix. The vaginal removal of such tumors in the absence of other fibroids in the body of the uterus is a safe and effective procedure.

**Hysterectomy.**—More patients with fibroids are treated by hysterectomy than by any other type of therapy. This operation is indicated in young women who have myomas that are giving rise to symptoms for whom childbearing is no longer desired, as well as for women who are approaching the menopause with symptomatic tumors that increase the uterus to the size of a four months' pregnancy or larger. Myomas that are associated with other pelvic conditions such as pelvic inflammatory disease or endometriosis are best treated by hys-

terectomy and removal of the other diseased organs. Tumors that cause pain or pressure upon contiguous pelvic structures—the urinary tract, the lower bowel or the veins—should be removed surgically. Rapid increase in the size of a uterine fibroid is indicative of benign or malignant degeneration and its removal is imperative. All postmenopausal tumors that are increasing in size or are giving rise to symptoms such as pain, bleeding or pressure upon contiguous structures should be removed surgically. Irradiation therapy is contraindicated for postmenopausal tumors.

Two approaches, the vaginal and the abdominal, are utilized for the removal of uteri that contain myomata. The *vaginal approach* is reserved in our clinic for uteri that are slightly enlarged due to myomas in the absence of adnexal disease and in the absence of previous pelvic surgical procedures. It is particularly applicable when small tumors are accompanied by pelvic relaxation that requires repair. Morecellation of fibroid tumors to permit vaginal removal is not recommended because of the hazards that attend this procedure.

The *abdominal route* is preferable as a general rule for it permits inspection and care of all the pelvic structures, palpation of the upper abdomen and it is a far less traumatic procedure. Two questions usually arise at the time of operation: that of supravaginal versus total hysterectomy and that of ovarian conservation. While we do not practice routine total hysterectomy we believe that it is indicated in the presence of benign cervical disease if the local situation and the constitutional condition of the patient do not contraindicate an operation that is considerably more difficult and one that will require at least 20 per cent more time. Should doubt exist it is far better to treat the benign cervical condition by curettage, biopsy and conization and to do supravaginal hysterectomy. The presence of extensive pelvic inflammatory disease or of pelvic endometriosis with cul-de-sac infiltration is a contraindication to elective total hysterectomy. Such general conditions as extreme obesity especially if the pelvis is deep, cardiovascular disease or chronic anemia serve as contraindications to elective removal of the cervix at the time of the hysterectomy. As to ovarian conservation it is our opinion that this tissue should be conserved if it is healthy and if it shows evidence of function in the form of a recent corpus luteum no matter what the age of the patient. Therapeutic estrogens are imperfect substitutes for the ovarian secretions and the risk of malignant degeneration of a conserved ovary is not sufficiently great to demand its removal. There is no definite age limit for conservation of functioning ovarian tissue. The decision depends upon the nervous system of the patient, the condition of the ovaries as observed at opera-



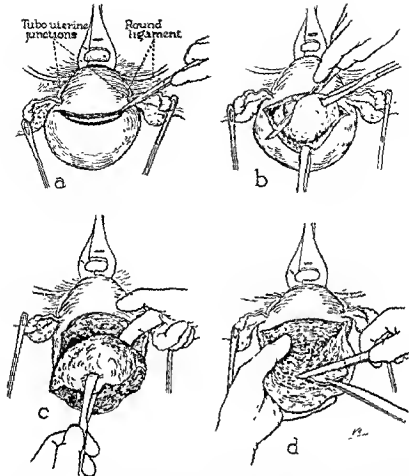


Fig 401 —Donney's "hood" operation for posterior fibroids of good size, designed to avoid a suture line on the posterior wall of the uterus where it lends itself to dangerous adhesion and, if oozing occurs, to blood among the intestines

a, A transverse incision is made  $\frac{1}{2}$  inch behind a line joining the tubo-uterine junctions. It should not extend into the ovario-uterine ligaments, or into the tissue immediately in front of them, to avoid cutting a number of large veins in these situations. The plane of cleavage between the fibroid and its capsule is sought for and when it is found it is opened up, using either the scalpel handle or, if the capsule is not resistant, the index finger. Great care must be exercised to avoid making a hole in the capsule when turning it off the fibroid, as the capsule is going to form the hood.

b, after the surface of the fibroid has been sufficiently cleared, the tumor is enucleated by morcellation. With a volsellum it is pulled out as far as it will come and a portion of it is cut off, taking care that the sharp edge of the scalpel is kept clear of the capsule. Another grasp with the volsellum is secured and the process is repeated until only the base remains.

c, If the attachment of the base is loose it can be removed entirely with the fingers as shown. The physician's left hand behind the uterus makes pressure on the mass to be removed. Another method is to roll it out, stroking off the adhesions by firm pressure with a swab. If the adhesion is strong the sharp edge of the scalpel can be used, keeping it close to the tumor so as not to pierce the capsule. Above all, the capsule must be preserved intact.

d, After the edge of the capsule or hood has been beveled with scissors to permit later

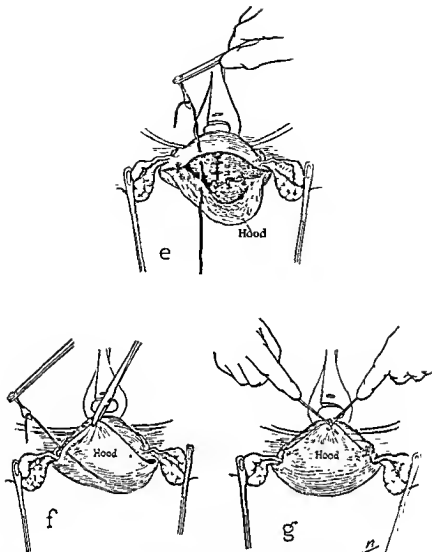


Fig. 401—Continued

The uterine cavity is now opened by a midline incision and explored with the finger to make sure that it contains no polypus, submucous fibroid, or other cause of abnormal bleeding. The wall is carefully palpated between the finger on the inside and the peritoneal surface. Any tumors found are removed by secondary incision. The incision is then closed. If the uterine wall is normal, the procedure is completed.

e. After trying the hood for size, by pulling it over the top of the uterus, to make sure that it is broad enough to cover the top of the uterus, a tier of interrupted catgut sutures is inserted low down in the uterine wall, meanwhile stretching upward on the hood with the left hand. One or two sutures may be required before making the tier which picks up the edge of the hood (as illustrated).

f. The hood is now brought over the top of the uterus, put in place on either side, over the tubes outside their junction with the uterus.

tion and many times the economic circumstances of the patient. Generally speaking, when there is doubt we prefer to retain ovarian tissue

The technic of hysterectomy is described in many standard textbooks and need not be given in detail here. Certain principles, however, may be mentioned. A preliminary curettage is done prior to every hysterectomy for fibroids in the event of intermenstrual bleeding. This will prove or disprove the presence of retained secundines, corpus carcinoma and endocervical carcinoma as well as submucous myomas. If a total hysterectomy is not planned a dilatation and curettage, biopsy and conization of the cervix should be done for every patient whether there is evidence of cervical disease or not. Following removal of the uterus, unless the cervix and adnexa have been removed the specimen should be opened and examined before the peritoneum is closed in order to rule out the presence of an early corpus carcinoma. If ovarian tissue is to be conserved it is well to save the accompanying fallopian tube to better preserve the integrity of the blood supply. Finally, the abdominal incision should be sufficiently large to permit removal of the tumor without trauma to the anterior wall and to the remaining pelvic structures. While it is probably true that some surgeon in a facetious moment stated that "the uterus was put in a woman's body to be removed," its removal may prove to be an exceedingly hazardous procedure. Preliminary examination under anesthesia is a great aid in predicting the difficulty that will attend a hysterectomy but even this is not dependable always. No surgeon should undertake an "easy hysterectomy" unless he is equipped with the training, the assistance and the physical facilities to finish the job if it turns out to be far more difficult than he anticipated.

### SUMMARY

The benign nature of uterine fibroids is such that their presence is not an indication for immediate active therapeutic measures. Methods of management of these tumors may be divided into four types: observation, hormone therapy, irradiation and surgery. Neither type competes with the other and each possesses clear-cut advantages and disadvantages. Conservatism in the choice of a plan and further conservatism in its execution are essential to the proper management of myomas of the uterus.

## THE SURGICAL APPROACH IN THE MANAGEMENT OF UTERINE DISPLACEMENTS

JOHN B. MONTGOMERY, M.D.\*

WHEN conservative methods have failed to control the distressing symptoms of uterine displacements and their associated lesions in women of childbearing age or when these conditions are encountered in later life some form of surgical treatment usually is advisable. It is wise to avoid operative treatment in younger women as a rule since subsequent pregnancies and deliveries occasionally may cause a recurrence of the lesion. Perhaps a more important reason for conservatism in this age group has to do with the responsibility of the young mother to her family. In many such instances the demands of young children and the lack of economic resources create a situation which may make it unwise for the patient to take the time away from her family and to assume the slight risk to health and life that always is associated with surgical correction. On the other hand, the symptoms of uterine displacement and associated lesions may interfere with the activities of the young housewife to such an extent that she cannot properly care for her children or adequately carry out her family duties. Under such circumstances, surgical treatment becomes imperative.

In women who are approaching, or who have passed the menopause, the annoying symptoms of uterine displacements and associated lesions should be relieved promptly by proper surgical correction, unless there is some contraindication to operation. Vaginal plastic procedures are well tolerated by women in the older age groups. We do not hesitate to advise operative correction of uterovaginal prolapse up to and occasionally beyond 70 years of age. One frequently encounters displacements of the uterus and pelvic floor relaxation of various degrees without symptoms in women of menopausal age. Such patients not infrequently seek operative treatment because they have the impression that these lesions, which are the result of the trauma of childbirth, may lead to carcinoma. In the absence of symptoms, it is wise to correct any cervical lesion that may be present but unless the other lesions resulting from the trauma of childbirth are obviously in need of cor-

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rection, it is wise usually to defer more radical surgical procedures until such time as the associated symptoms or the progressive increase in the displacement provides a more definite indication for surgery. Although these symptomless lesions often become progressively more pronounced as the atrophy incident to the menopause and advancing years progresses, this is not always the case. In some instances the shrinkage associated with the atrophic changes of the menopause may influence favorably the lesser degrees of pelvic floor relaxation.

Although much progress has been made in the development of various operative procedures for the management of uterine displacements and other lesions incidental to birth trauma, and some methods have now gained favor over others, no standardized procedure is available for the routine treatment of all cases, nor should it be so. In each individual patient the need for operation and the type of operation to be done must be decided on the basis of the various factors involved, i.e., the age of the patient, the advisability of maintaining menstrual function, the possibility of future pregnancies, the physical condition of the patient, the type and degree of uterine displacement and the presence of associated lesions.

### RETRODISPLACEMENT OF THE UTERUS

In many instances retrodisplacement produces no symptoms and requires no treatment. This applies especially when the displacement is congenital or when it follows pregnancy in the absence of associated pelvic floor relaxation, descensus, subinvolution, varicosities of the broad ligament or adnexal disease. Symptoms due directly to the retrodisplacement are most commonly referred to the lower abdomen or suprapubic region as a heavy pressure or bearing down feeling and to the lower back as a dull sacral backache. Both of these symptoms are relieved by the recumbent position and aggravated by exertion. Dyspareunia and functional menstrual disturbances may be present due to associated prolapse of the ovaries and disturbances in their circulation. *Symptoms referable to the bladder and rectum may occur also.* Occasionally sterility and spontaneous or repeated abortion may be attributable to the displaced uterus.

Proof that these symptoms are due to the displacement is forthcoming when the uterus is replaced manually and maintained in position by a Smith or Hodge pessary. This can be successfully carried out in almost all instances where the uterus or adnexa are not adherent and should be done routinely as a therapeutic test before surgical treatment is decided upon. This plan may be carried out over a long period of time with very little discomfort to the patient. In occasional

instances no further treatment is necessary, although as a rule the pessary is only palliative. Findley reported 75 per cent of cures in primipara and 25 per cent in multipara when the retroversion was corrected and a special type of Smith pessary was inserted within ten to fourteen days after delivery.

**Operative Treatment.**—When such a plan is unsuccessful or when it is poorly tolerated we do not hesitate to carry out surgical treatment of this lesion during the childbearing period. We prefer a combined vaginal plastic procedure (conservative anterior and posterior colporrhaphy) and uterine suspension in women of this age. We believe that the Simpson or Montgomery modification of the Gillian round ligament shortening operation is the best technic for uterine suspension for several reasons. It utilizes the strong muscular portion of the ligament near the uterus which will hypertrophy with pregnancy and involute following delivery. There is no trauma to the exposed peritoneal surfaces and hence little likelihood of postoperative adhesions. The supporting round ligament is firmly anchored to the under surface of the anterior sheath of the rectus and also becomes adherent throughout its extraperitoneal course, assuring firm support. There are no adventitious openings through which the intestine might pass, resulting in obstruction. The operation is simple and easy to perform, with a minimum of trauma to tissues. When the cervix is descended into the vagina, uterosacral shortening is sometimes carried out also, but as a rule this is not necessary.

Several details in the technic of the Simpson operation are important for its success (Figs. 402, 403, 404). The small incision in the anterior sheath of the rectus fascia should be made about 1 inch from the midline and on a level with the internal inguinal ring. When the round ligament is drawn upward to the rectus fascia through the small opening made in the anterior leaflet of the broad ligament peritoneum, the opening in the peritoneum should be large enough to prevent constriction and possible strangulation of the ligament. Before attaching the round ligament, the limb of the loop nearest the uterus should be carefully examined to make sure that its length will hold the fundus at the proper level. When the loop of round ligament is attached to the rectus fascia the sutures should be passed through the ligament superficially in order to avoid injury to the central artery.

Among 489 patients operated upon by this method Anspaeh and Montgomery reported operative complications in three cases. Hemorrhage occurred into the broad ligament in two patients and in one there was bleeding from the deep epigastric vessels. The bleeding was readily controlled in each instance although in one case it was neces-

sary to remove a tube and ovary. Three hundred and forty-eight patients were followed from six months to several years after operation. In 343 of these the uterus was found to be in normal position. Sixty-one patients had been delivered at term (five by cesarean section) and in three of these the uterus was in retroversion and descensus of the first degree.

When it is necessary to remove a tube and ovary in conjunction with uterine suspension we prefer to cover the raw area on the cornu of the uterus by posterior fixation of the round ligament on the affected side and carry out the Baldy-Webster or the Simpson round ligament short-

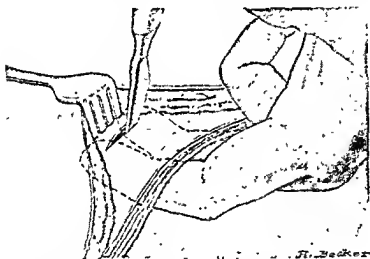


Fig. 402.—Simpson operation. The skin and fat are retracted and freed from the fascia of the rectus muscles on both sides of the lower extremity of the abdominal incision, slightly below the level of the internal ring. The fascia is incised about one or two centimeters from the median border of the fascia on each side, the fingers inside the incision giving support. (Anspach, Gynecology, J. B. Lippincott Co.)

ening operation on the opposite side (Figs. 405, 406). When, because of fixation of tissues and consequent shortening of the round ligaments, the Simpson operation cannot be done, the Baldy-Webster round ligament shortening technic is the procedure of second choice. Care must be taken to attach the round ligaments at the proper level on the posterior surface of the uterus and to close the opening in the broad ligament peritoneum snugly around the round ligament. We do not believe that this procedure will withstand pregnancy and labor as well as will the operation that utilizes the uterine or proximal portion of the round ligament for uterine suspension. We have had little ex-

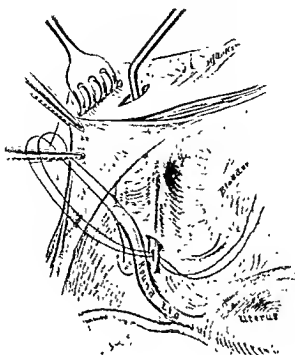


Fig. 403 —Simpson operation. A specially curved needle is now passed through the fascial cut, between the muscle bundles to the peritoneum, beneath this to the internal ring, then under the peritoneum of the anterior leaflet of the broad ligament and through the peritoneal cut. The traction suture ends are then threaded through the eye of the needle, which is withdrawn (Anspach, Gynecology, J. B. Lippincott Co.)

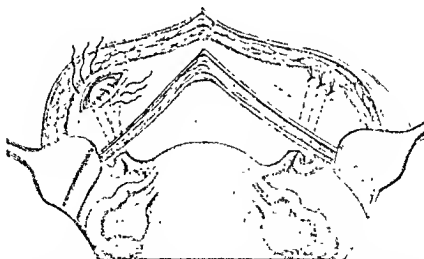
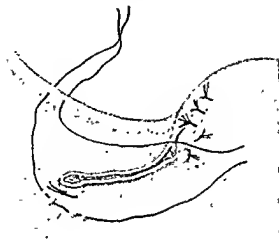


Fig. 404 —Simpson operation. The round ligaments are sutured to the under surface of the fascia by three interrupted sutures of fine linen or catgut. These also close the fascial incision (Anspach, Gynecology, J. B. Lippincott Co.)



perience with the Coffey operation which suspends the uterus by plicating the proximal portion of the round ligaments and broad ligament peritoneum on the anterior surface of the uterus. It is very popular



*H Becker*

Fig 405—Salpingo-oophorectomy Peritonealization with posterior fixation of the round ligament (Anspach, Gynecology, J B Lippincott Co)

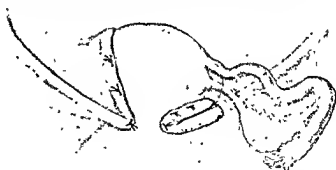


Fig 406—Salpingo-oophorectomy Posterior fixation of round ligament with peritonealization, on opposite side Webster-Baldy operation (Anspach, Gynecology, J. B Lippincott Co)

in some clinics, but in our judgment the trauma to the peritoneum makes this procedure inadvisable except in certain special instances where the other technics cannot be utilized. Olshausen's technic

utilizes the most desirable portion of the round ligament but its attachment to the peritoneum may be insecure and is associated with local trauma which in some instances may result in intestinal or omental adhesions. The bladder advancement operation of Curtis has not been utilized by us except in occasional instances where it seemed advisable in order to cover raw surfaces on the anterior uterine wall.

When in the occasional patient surgical treatment of retrodisplacement of the uterus is necessary in women approaching the menopause, we usually perform hysterectomy (total or subtotal), especially if the uterus is large and boggy, in preference to suspension of the uterus unless the patient's condition or other factors make the more extensive procedure inadvisable.

### PROLAPSE OF THE UTERUS

During the last two decades appreciation of the importance of the cardinal (Mackenrodt's) ligaments in maintaining the uterus at the proper level in the pelvis and the development of the Manchester-Fothergill operation have greatly simplified the surgical management of uterine prolapse. Maier and Thudium, whose report of 138 cases (Fothergill operation) in 1932 antedated the paper of Fletcher Shaw of Manchester popularizing the operation in this country, advocated this operation as a standard procedure for all patients with prolapse of the uterus. Their report included forty-seven women of childbearing age, thirteen of whom became pregnant and delivered without dystocia or subsequent recurrence of their uterovaginal prolapse. It was their opinion that this operation does not interfere with pregnancy and labor if 3 inches of uterine canal is retained in those patients in whom the cervix is amputated. Shaw stated in 1933 that "there is a tendency for us to defer this operation until the patient has reached an age when she is not likely to have more children or when she has made up her mind that she has as many as she desires." He reported only twenty-seven women who had subsequent pregnancies and delivery among 549 who had been operated upon. Five of these showed signs of recurrence. However he apparently considered the operation satisfactory for women during the childbearing period as he concludes that "it is the best method of treatment for all cases of prolapsed uteri." Gordon in 1946 reviewed the literature and noted that among 2837 patients operated upon by the Manchester operation, 551 were in the childbearing age. Two hundred and forty were delivered later and forty of these developed recurrence of the prolapse.

In our own experience, this operation has proved highly satisfactory

in a large majority of patients over 40 years of age who have first or second degree prolapse (first degree, cervix at vaginal introitus; second degree, cervix outside introitus) We do not depend upon it when the uterus is in the third degree of retroflexion, especially if the fundus is enlarged We have not used it when pregnancy was likely to occur later, so that cervical amputation has been a part of our technic almost routinely. Although subsequent pregnancy apparently is not adversely affected in most instances, in our opinion the possibility of abortion or dystocia makes the use of this procedure unwise during the childbearing age. In such instances we prefer to perform the more conservative vaginal plastic operation with uterine suspension Most gynecologists prefer vaginal hysterectomy in patients with third degree prolapse (procidentia) We concur in this view since removal of the small uterus that is completely outside the vagina facilitates the approximation of the cardinal ligaments in support of the vaginal vault. In performing this operation for procidentia we remove the uterus between clamps as in the Mayo technic, but use separate suture ligatures to control bleeding and to unite the broad ligaments Special attention is paid to uniting the uterosacral ligaments to prevent development of a cul-de-sac hernia, and to plicating the fascial supports of the bladder and the urethra.

**Operative Technic.**—As TeLinde has stated, "the Manchester operation is simply a radical anterior colporrhaphy" Essential for its success is a wide exposure of the cardinal (Mackenrodt's) ligaments and a wide separation of the pubocervical fascia from the vaginal mucosa (Fig 407). The extent of the dissection of course, depends somewhat upon the degree of prolapse and the size of the associated cystocele Elevation of the uterus in the vagina is dependent primarily upon shortening of the cardinal ligaments by plicating them on the anterior surface of the cervix Wide plication of the pubocervical fascia in the midline is an important part of the technic also since it not only corrects the associated cystocele, but supplements the uplifting effect of the shortened cardinal ligaments Care should be exercised also to support the neck of the bladder and the urethra by carrying the anterior wall plication well forward.

Most of the published illustrations, including those of Shaw, fail to show clearly the wide dissection that is necessary in order to assure adequate shortening of the cardinal ligaments and wide plication of the pubocervical fascia In our experience, moderate overcorrection of the fascial relaxation assures the best results This may cause narrowing of the vagina occasionally, but a little experience enables one to guard against this disadvantage When placing sutures in the anterior vaginal wall following the wide fascial dissection it is possible to injure the ureters. This danger can be avoided by always passing the sutures through the

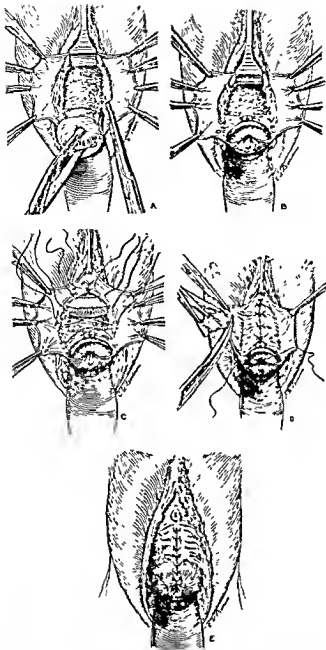


Fig 407 —Manchester operation for uterine prolapse and cystocele *A*, Bladder has been dissected up from cervix Incision has been carried through mucosa around cervix and mucosa dissected free from cervix Bases of broad ligaments are thus exposed The left has been clamped and cut Dotted line indicates where cervix is to be amputated *B*, Cervix has been amputated and posterior lip covered with flap of mucosa The bases of the broad ligaments have been sutured to the anterior surface of the cervix *C*, Pubo-vesico-cervical fascia is being approximated in the midline beneath the urethra, base of the bladder and the cervix Note that the lower sutures bite into the anterior wall of cervix *D*, left, Fascia approximation has been completed Excess vaginal mucosa is being excised The first suture has been placed through flaps of mucosa, biting into cut surface of the shortened cervical lip to cover it with mucosa *E*, Operation on anterior wall has been completed It is to be followed by a posterior colporrhaphy (Telande, *Operative Gynecology*, J B Lippincott Co)

fascia superficially. If the bladder is inspected cystoscopically after the wide plication of the supporting fascia the trigone usually will be seen to be pushed forward, forming a prominent ridge. This deformity causes no permanent trouble and usually disappears spontaneously after four to six weeks. Subsequent observation of the bladder should be carried out in order to guard against faulty drainage or other disturbances that may lead to annoying symptoms later.

Repair of the posterior vaginal wall in connection with the Manchester operation sometimes presents difficulties when an enterocele or high rectocele is present. In dealing with the enterocele it is well to extend the dissection upward to the uterosacral ligaments where these structures can be approximated in the midline. If a large peritoneal sac is present it must be excised, however in less extensive cases opening the peritoneum and excision of the sac is not necessary. The dissection is carried up behind the cervix and the fascia of the uterosacral ligaments is united extraperitoneally. In order to support the upper portion of the posterior vaginal wall, we formerly sutured the fascia overlying the superior surface of the levator ani muscles together in front of the rectum at as high a level as possible. This sometimes resulted in narrowing the vagina (more common after the Manchester operation repair of the anterior vaginal wall), and in some instances was not successful because of the tension required to bring these structures together at this level. At present, we are able to secure satisfactory support of the upper part of the posterior vaginal wall by utilizing the posterior vaginal fascia. This is found as a thin attenuated layer lightly attached to the posterior vaginal wall. It may not be present due to attenuation near the midline, but always can be demonstrated laterally. It is easily separated from the vaginal mucosa by blunt dissection and its plication from side to side in the midline provides firm support for correction of the high rectocele.

The Watkins interposition operation was regarded as a very satisfactory method of treating minor degrees of prolapse associated with cystocele in our clinic previous to the advent of the Manchester operation. In recent years it has been discarded. Ventral fixation of the uterine fundus has also been discontinued. In very elderly or debilitated women in whom it is not necessary to maintain a functioning vagina, the LeFort method of colpocleisis performed under local anesthesia has proved very useful. It is best adapted to those cases with fairly good perineal support. If this is lacking it is wise to reconstruct the perineum in order to facilitate approximation of the anterior and posterior vaginal walls all the way down to the vaginal orifice. We have had no experience with the Spalding-Richardson composite operation, but the results of these authors as well as those of TeLinde and others indicate that it is a valuable procedure in selected cases.

## SUMMARY

The surgical treatment of uterine displacement provides the only means of permanent cure for these patients. Its successful practice calls for an understanding of the anatomical factors that maintain the normal position of the uterus and a knowledge of the operative procedures that are adaptable to the various circumstances that may be encountered. Operations are available for the management of this lesion during the child-bearing years, at the age of the menopause or in the woman of advanced years. No operation is suitable for all cases. Best results are obtained when each patient is individualized and the operative procedure carried out as indicated by the factors involved in each case. In our hands the most useful procedures have been anterior and posterior colporrhaphy with uterine suspension by the Simpson technic, the Manchester-Fothergill operation and LeFort colpoceleisis or some modification of these technics.

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# VENOUS THROMBOSIS IN OBSTETRICS AND GYNECOLOGY\*

J. EDWARD LYNCH, M.D., F.A.C.S.\*

THE serious implications of the intravascular clotting of blood, or thrombosis and the potential sequel pulmonary embolism with all its immediate and eventual complications, is well recognized by most physicians and surgeons. A discussion of the various factors inherent in this condition, its prevention, diagnosis and active treatment, may be of some value.

## CLASSIFICATION

The intravascular clotting of blood, or thrombosis, may be subdivided into two general headings

**Phlebothrombosis.**—In phlebothrombosis or venous occlusion, the clot develops in an ascending fashion, beginning in the capillary bed and extending centrally into the larger collecting venules and veins. It is not associated with any inflammatory process in the intima of the vessels, and is only loosely attached to the walls of the vessels in which it propagates. Such areas are silent and usually unproductive of definite symptoms or signs unless suspected and looked for and the insidiousness of the entire process makes it by far the more dangerous to the life of the patient.

**Thrombophlebitis.**—In thrombophlebitis or venous occlusion the process of clot formation is associated with or secondary to inflammation of the vein wall. The clot is usually quite firmly attached to the intima, and may propagate centrally or peripherally inasmuch as the process usually develops not in the capillary bed but in the lumen of one of the veins. Such a condition, when it develops, is not silent but on the contrary produces local tenderness, pain, fever, and evidence of obstruction to the venous drainage of the part, particularly when a larger vessel is involved. It is likely that this represents the end stage of the process, the silent thrombus formation or phlebothrombosis representing the primary stage of venous thrombosis. Aside from thrombophlebitis developing in varicose veins, this condition more often occurs in the larger vessels, greater and short saphenous and especially the iliofemoral veins and pampiniform plexus of veins in the pelvis

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## PATHOGENESIS

Intravascular clot formation is favored by several factors some of which can, to a greater or lesser degree, be influenced by careful pre-operative study and preparation and post-operative care. They are:

1 Factors which slow the circulation in the venous system (even more than the normal slowing due to the increased resistance of the greater surface area of the capillary bed) such as: cardiac failure incipient or actual, mild to moderate degrees of hypertension, hypothyroidism and myxedema, polycythemia and extrinsic pressure over the calves of the legs or constriction of the extremities at any level due to the position the patient occupies in bed

2. Anything which causes increased coagulability of the blood, seen usually after hemorrhage, or trauma associated with surgery or injury to tissue as with abruptio placentae. Conceivably the presence of excessive amounts of adrenalin in the circulating blood secreted in an overly anxious postoperative patient could be sufficient to throw the balance in favor of thrombosis in an individual in whom other factors operating in favor of intravascular coagulation were present. The significance of the so-called "blood sludge" now being studied and its relation to increased coagulability of the blood may be an important factor in some individuals

3 Changes in the intima or lining of the vessels of the venous (or arterial) systems such as local trauma infection surrounding a vessel, and chemical inflammation following the intravenous injection of hypertonic solutions or others not intended for that method of administration.

## PROPHYLAXIS

Prophylaxis against intravascular clotting of blood is the keynote of success in all fields of medicine and particularly in obstetrics and gynecology. It is to be remembered that every patient is a possible candidate for this condition but certain patients are not only possible but very likely candidates if a careful plan of management is not established and followed. For example, a patient giving a history of previous intravascular clotting has possibly about a 10 per cent chance of a recurrence with subsequent surgery if prophylactic measures are not carried out pre- and postoperatively. Patients showing marked obesity with or without obvious hypothyroidism or myxedema call for investigation of their metabolism and medication to increase it if it is low. Those patients exhibiting extensive systems of markedly distended and tortuous varicose veins in the legs not infrequently harbor small mural thrombi which develop secondary to irregularities in the vessels and eddies in the current of the circulating blood. Following superficial trauma such areas may be

the focus for a propagating thrombus, the tail of which may become disengaged producing a pulmonary embolism before complete fixation to the intima of the vessel has taken place. Adequate fluid intake pre- and post-operatively is necessary to prevent dehydration and consequent increased viscosity of the blood which favors slowing of the circulation in the smaller vessels.

Under prophylactic measures should be mentioned the following:

1. **Watchfulness of Attendants for Early Signs.**—The medical personnel must be educated to be on the lookout for early signs. Nurses should report such "minor complaints" as cramp in the foot or in the calf of the leg in postpartum or postoperative patients. The importance of frequent checking of legs and feet for normal warm, dry sensation or suggestive cold, clammy sensation seen in association with impaired circulation often as a precursor to vascular thrombosis must be stressed. Foreible dorsiflexion of the foot at the ankle to determine tenderness in calf muscles (Homans' sign) and careful palpation of the calf muscles and tissues over the deep vessels to elicit areas of tenderness are useful measures.

2. **Position of the Patient.**—The position occupied by the pre- or postoperative patient in bed may be a significant factor in favoring or counteracting a tendency to thrombosis. It is recognized, as mentioned above, that slowing of the circulation can favor intravascular clot formation. The patient who is made to appear neat by being propped up in bed with a back rest and with support under the knees and calves may be quite comfortable. However, such a position restricts the activity of the patient—she is so comfortable that the thought of changing position does not occur to her. The result is that an important factor in the maintenance of the venous circulation, muscular activity, is more or less eliminated. It is recognized that the circulation is maintained primarily by contractions of the left ventricle but this is aided and abetted by the negative pressure developed in the thoracic cavity as the accompaniment of deep breathing, the action of the right side of the heart and the massaging effect of the skeletal muscles on the veins in proximity to those muscles. Hence it follows that the propped-up comfortable patient can or is likely to do little to aid in the circulation of her blood. It is far better for a patient to remain in the horizontal position in bed to kick her legs up and down, from side to side, and back and forth, and to change position herself by rolling and turning from side to side. Especially should she be encouraged to inspire as deeply as she can as often as she thinks of it.

**Early Ambulation.**—Early ambulation after delivery and pelvic surgical procedures has been shown to help reduce the incidence of venous thrombosis. Its mode of action presumably is in the aid and stimulation it provides to the general circulation and venous blood flow, in particular.

Active movements of the extremities by the patient while in bed serve as a useful adjunct or even a substitute for early ambulation, especially when combined with frequent deep inspiration or forceful exhalation. To obtain the latter patients may be encouraged to inflate balloons or "blow up" paper bags. This procedure, incidentally, is of great value in distending the lungs and aids in preventing and overcoming postoperative pulmonary atelectasis.

**Patients with a Previous History of Intravascular Clot Formation.**—In these cases, in addition to the usual preoperative laboratory studies, the so-called clotting factors are estimated, viz., skin bleeding, coagulation and prothrombin time and total serum protein with albumin-globulin ratio. A member of the hematologic division of the department of medicine is asked to see the patient in consultation and a decision is made as to whether the patient is to be treated with one of the chemical anticoagulants in current use, heparin or dicumarol, preoperatively or beginning twenty-four to forty-eight hours postoperatively. When anticoagulants are used preoperatively the possibility of increased bleeding at the time of surgery is anticipated, making extreme care in hemostasis during the operation mandatory as well as having suitable blood available for transfusion. More commonly, the medication is given postoperatively, starting after the first twenty-four hours. Heparin, when used, is in 50 mg (0.03 gm) doses intravenously every fourth hour during the first forty-eight hours of treatment. This method is used for its more rapid effect in prolonging the coagulation time. Its mode of action is not definitely known. At the same time, dicumarol is started, to be continued for a more prolonged period of time. Three hundred milligrams (0.3 gm) are given the first day, 200 mg (0.2 gm) the second day, and 100 mg (0.1 gm) the third and successive days depending on the need as indicated by the degree of lowering of the prothrombin time and consequent prolongation of the coagulation time. Usually, as a prophylactic measure, a level of 60 per cent of normal is satisfactory but if evidence of active clot formation is present, this level must be lowered to about 30 per cent of normal.

Active treatment will be discussed under a separate heading later. At this point it may be stated that it is usual for ligation to be carried out when a definite diagnosis of thrombosis is made in the postoperative or postpartum patient. We usually do not wait for the patient to show signs of pulmonary embolism before ligation is carried out.

#### **PATHOLOGY OF INTRAVASCULAR CLOT FORMATION**

Only the pathology of the terminal stage i.e., after the thrombus has formed, is known. Pathologists describe three kinds of thrombus—red

or coagulation thrombi, white or agglutination thrombi and a mixed type which is the form most commonly encountered. The theory of the development of a mixed thrombus is clearly and concisely described by Allen, Barker and Hines and is quoted with their permission.

As a result of slowed flow and eddy currents in the venous blood stream plus changes in platelet-plasma stability, the platelets tend to accumulate in the slower moving periphery of the stream and stick to the endothelium. They may stick only at the site of a pre-existing lesion of the endothelium but such lesions are probably not necessary particularly in the secondary type of thrombophlebitis [those seen after trauma, surgery or in postpartum state]. The platelets tend to disintegrate, leukocytes are attracted and a small amount of fibrin is precipitated. These events are followed by the deposit of more platelets, fibrin and leukocytes in layers. The deposits usually progress in a distal direction. The white head of a mixed thrombus may or may not occlude the lumen of the vein. The red tail develops in a proximal direction, that is, toward the heart. It may be a homogeneous red coagulation thrombus but frequently it is a lamellated deposit of layers of leukocytes, platelets and fibrin interspersed with layers of erythrocytes and fibrin. It is probable that increased coagulability of the blood even though slight is the chief factor responsible for the development of the propagating tail of the thrombus. The tail probably develops rapidly, for sections through various portions of a red or lamellated thrombus are similar in appearance. However, its consistency and cohesion may be variable in different cases. In some instances it is firm and fills the vein; in others it is more friable and does not completely occlude the lumen. The red or lamellated tail of the thrombus tends to adhere to the endothelium rather soon after it forms and when this adherence occurs, organization by fibroblasts from the endothelium follows rapidly and completes the adhesion.

Phlebothrombosis, as it develops in some of the smaller venules and veins in the substance of the plantar or calf muscles, is presumed to be the primary condition. This is the acute or early phase of which our knowledge is deficient. It is known that once a thrombus has formed in a vessel, organization of the periphery of the thrombus from fibroblasts originating in the intima soon takes place at their points of contact, thus fixing the thrombus to the vessel wall. Subsequently, the symptoms and signs of thrombophlebitis develop in the vessel following the organization and attachment of the thrombus. The conclusion, of course, is that frequently the insidious phlebothrombosis is the precursor of the symptom-producing thrombophlebitis and it is only when the full-blown condition is present that the phenomenon of intravascular clotting or so-called venous thrombosis is recognized. By this time the danger of pulmonary embolism, the most feared complication of silent thrombus formation or phlebothrombosis, has largely passed. A propagating tail developing after

the fixation of the primary thrombus may, however, be the source of a pulmonary embolism which may or may not be fatal depending on its size.

### DIAGNOSIS

Actually, in speaking of the differential diagnosis of phlebothrombosis and thrombophlebitis, which we consider to be two stages in the same process, we are endeavoring to distinguish between early and late diagnosis of venous thrombosis. When the stage of a full-blown thrombophlebitis has been reached, the diagnosis becomes self-evident because of the of the late symptoms, viz., fever, elevated pulse rate, pain and localized tenderness with the indurated thrombosed veins being frequently easily palpable, especially in instances of involvement of the more superficial veins. Naturally, we are anxious to establish an earlier diagnosis of phlebothrombosis and we ask ourselves the question, "How can we do this?"

The diagnosis of phlebothrombosis is accomplished, first, only by considering the condition of thrombosis as a possibility in all post-operative and postpartum patients, and secondly, by looking for evidence of the few telltale signs of beginning impairment of the peripheral circulation especially in the legs. When actual impairment of the circulation has developed, the condition has progressed to the later stages of venous thrombosis, namely thrombophlebitis.

The signs and symptoms we should anticipate are as follows:

1. The complaint of a cramp in the plantar region of the foot, soreness of the heel, tightness about the ankle or stiffness or cramp in the calf muscles of the leg

4. Change from the usual warm dry or slightly moist skin of the feet and lower leg to a definitely cool or cold wet skin, sometimes with mottling of the skin.

3. Definite discomfort or pain in the plantar muscles on manipulation of the foot or in the calf muscles when pressure is made over them

4. Homans' sign, which is elicited by the forcible dorsiflexion of the foot. When it is positive, the patient complains of a tightness or pain in the calf muscles. The fact that the test is negative is of little significance while a positive sign is at least suggestive if no other obvious pathologic condition is present.

5. Palpation of the pulsation of the dorsalis pedis artery. Usually a full wave is felt but when spasm is present it is almost imperceptible. We know that vascular spasm is associated with venous thrombosis. Through its effect in reducing the lumen of the vessels, it reduces the volume of circulating blood. Such an effect when passed on to the capillary bed and the venous system can be seen to contribute to stasis and thrombosis

6. Laboratory studies to demonstrate an increased coagulability of the blood are in order when the above suggests the possibility of beginning venous thrombosis. If these are corroboratory then it is wise to begin active treatment aimed at improving the peripheral circulation of the legs and lowering the coagulability of the blood with or without ligation of the major veins of the leg (s).

### ACTIVE TREATMENT

The diagnosis of early venous thrombosis having been at least tentatively made and confirmed by observation and laboratory studies which demonstrate increased coagulability of the blood, active treatment is instituted. As indicated above this treatment aims at:

1. Lowering the coagulability of the blood by the use of anticoagulants such as heparin and dicumarol and maintaining adequate fluid intake to prevent dehydration.

2. Improving the blood flow through the vessels of the legs by parasympathetic block for unilateral conditions or continuous spinal anesthesia for bilateral conditions. A satisfactory response from these measures is subsidence of the pain and tenderness and restoration of warmth and color to the involved parts.

3. Interruption of the continuity of the venous system at the desirable level when a definite diagnosis of phlebothrombosis has been made or if nonfatal pulmonary embolism has developed in spite of measures 1 and 2 above.

Venous thrombosis is regarded at the Jefferson Hospital as one of the major complications in the postoperative and postpartum state and the aid of medical and surgical consultants is requested early in the active management of the complication. Usually anticoagulants are given under the guidance of a member of the hematology department according to the manner and with the precautions listed under prophylactic measures aimed at preventing venous thrombosis. The surgical management (ligation of the vein with aspiration of the thrombus) is usually carried out by the surgical consultant at the level considered safest and best suited to the individual patient—femoral vein, common iliac vein or even the inferior vena cava if repeated pulmonary embolism has occurred after primary femoral or common iliac vein ligation. Anticoagulant therapy is of course continued even after ligation at any of the above mentioned levels. It is recognized that different opinions are held as to the desirability of venous ligation in the active management of venous thrombosis, especially when it is complicated by pulmonary embolism, but it is the purpose of this paper to express the views held in the department of gynecology and obstetrics in the Jefferson Hospital

and not to enter into any discussion of the relative merits of any one program of treatment in contrast to another.

### SUMMARY

We consider that venous thrombosis is a generic term which includes both phlebothrombosis and thrombophlebitis, that in many instances the former represents the early stages of the process and the latter represents the full-blown end stage of venous thrombosis.

Prophylaxis is highly important but early recognition of phlebothrombosis with immediate institution of active treatment aimed at lowering the coagulability of the blood and increasing the circulation through the involved extremity is equally important. The dangers of the major complication of venous thrombosis, pulmonary embolism, are largely dissipated after the process has reached the stage of thrombophlebitis except in occasional instances.

When nonfatal pulmonary embolism develops in spite of anticoagulant therapy, venous ligation at the appropriate level is favored.

Finally, it is felt that this complication is of such a serious nature that the aid of medical and surgical consultants in its management is desirable from the time of its recognition.

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# THE INTELLIGENT USE OF SURGERY IN PELVIC INFLAMMATORY DISEASE

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## INTRODUCTION

THE term *pelvic inflammatory disease* is so broad in scope that discussion of all the infectious processes of the female genitalia under this one heading would lead only to confusion. It has been a common failing among doctors to be rather loose in their use of this phrase when making a diagnosis. There is a great difference between gonorrheal and cellulitis infections of the female genitalia. It is obvious, then, that the medical and surgical treatment is quite different in each case. The illuminating work of Arthur H. Curtis has provided the groundwork for our modern concept of pelvic infections

**Definition.—Gonorrhea.**—Gonorrhea is an acute infectious disease that attacks the lower genital tract first and spreads along the endocervical and endometrial canal to the tube and the pelvic peritoneum. After an initial or recurrent attack there is often a mixed infection present, spreading as though the gonococcus was the sole etiologic factor.

**Pelvic Cellulitis.**—The cellulitis group of pelvic infections makes up a more common and much more dangerous clinical entity than the gonorrheal cases. Included in this group are those infections caused by various streptococci, staphylococci, *B. coli* and almost any other pathogen known to us now. Criminal abortion, puerperal sepsis, and instrumental perforation of the uterus are the likely etiologic processes. In contrast to the mucous membrane spread of gonorrheal infection, cellulitis attacks first the uterus where the lymph and blood vessels disseminate the bacteria through the uterine wall to the surrounding structures. For example, the tube will usually show a perisalpingitis with cellulitis as contrasted with the endosalpingitis of gonorrhea.

Keeping these two clinical entities with their vastly different pathologic pictures before us, it is readily understood why the therapy and need for surgery is quite diverse.

## ACUTE GONORRHEA

We shall first consider the surgical needs of the patient with *acute gonorrhea of the lower genital tract*, i.e., urethra, Bartholin or vulvovaginal

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glands and cervix. The *urethra* is usually the site of first infection. If treated promptly with penicillin and the regular rules of hygiene are followed, the infection clears up promptly. There is no need for surgery in the usual acute gonorrheal urethritis. In the average case of acute gonorrhea, the *cervix* is almost as frequently involved as the urethra with the initial infection. All the characteristics of acute infection are present. The lesion should not be actively treated at this point but reliance placed on penicillin therapy. Actually, treatment with caustics or cautery during this phase will often result in strictures of the endocervical canal and, more serious, will cause upward extension of the disease. For this reason cervical therapy is contraindicated at this time.

The vulvovaginal glands are involved with the initial acute process far less frequently than one would expect. When it occurs the result is fulminating in character, for the acutely swollen, red, agonizing tender gland will rupture spontaneously about the time the patient sees her doctor. If rupture does not take place, incision and drainage should be instituted at once. Further attempt at treatment of the diseased gland should not be undertaken during the acute phase of the infection.

When gonorrhea spreads beyond the cervix we speak of it as an *upper genital tract infection*. In this upward spread, the endometrium becomes infected and we have a transitory acute endometritis. Since the ultimate goal of the infection is the adnexa and adjacent peritoneum, acute endometritis is so short-lived that it is of no surgical concern. During the upward spread, all the commanding signs of an acute pelvic catastrophe are present. Many a patient with acute salpingitis has been operated upon for acute appendicitis, ruptured ectopic pregnancy and similar conditions. Careful history taking and painstaking search for evidence of lower genital tract infection would have prevented most of these operations. Nevertheless, an occasional honest mistake will be made, and the operator finds himself faced with acute salpingitis. There is no reason to disturb the disease process at this time, in fact, it is definitely contraindicated. A million units of penicillin or 5 gm. of sulfanilimide crystals should be deposited over the acute adnexa, and the abdomen closed without drainage. There is no reason in the face of acute adnexal disease, to remove any of the involved tissue since spontaneous recovery is to be expected. Furthermore, a very high percentage of cases will never need surgery or at most a conservative, reconstructive procedure long after the acute phase has passed.

One might expect the formation of an abscess in the cul-de-sac in acute upper genital gonorrhea. If this occurs we have never seen a case. A purulent collection in the pouch of Douglas would lead us to believe

we were dealing with more than gonorrhea, most likely a mixed infection.

In summary, then, we would like to emphasize that *surgery is not needed in acute gonorrhea except for the drainage of Bartholin abscesses.*

### RECURRENT GONORRHEA

All too often patients who have had one attack of gonorrhea become reinfected. The picture after many such attacks has been referred to as chronic gonorrhea; however, a much more applicable term is recurrent gonorrhea. Such a disease entity is not confined to the prostitute, promiscuous or indiscreet, but finds its greatest incidence in the unenlightened dregs of society. These facts influence many surgeons in the choice of operations, or rather their lack of individualization in caring for these unfortunates. It must be remembered that these patients are human beings and as such have a right to the best that we can give in medical care.

**Lower Genital Tract.—Urethra.**—The urethra generally demonstrates purulent material on stripping. The infection is lodged deeply in the paraurethral gland structure. One can readily see with what a major lesion he is dealing by a careful survey of Huffman's article<sup>2</sup> describing the anatomy of the paraurethral ducts. We have seen some of these cases develop rather large abscesses, formed no doubt by a fusion of infected ducts, so that a single sac is formed between the urethra and vagina. The only satisfactory treatment is a longitudinal incision starting at the urethral meatus (cutting through the urethral wall and anterior vaginal wall) down to the base of the abscess. The starting point is "six o'clock" on the meatus. With the urethra and vaginal wall open, the wound edges and deeper lateral tissue should be coagulated with an electro-coagulating needle. No sutures should be used and the incised area should be left open for drainage and formation of granulation tissue. The patients are not incontinent, are comfortable and have little if any disability. Hot sitz baths for two weeks are an aid to healing which is usually complete by three weeks. Minimal paraurethral duct infection found just inside the meatus responds to desiccation with an electro-coagulating needle put directly into the areas that are thickened, no incision being necessary.

**Cervix.**—Chronic gonorrheal cervicitis is probably a more common lesion than we realize since cultures are usually negative. Whatever the etiology of the cervicitis it should be treated adequately. Since most of the patients are young the most satisfactory treatment is electrocautery. The portio vaginalis if markedly involved may be cauterized in stages.

The endocervical canal may be safely cauterized but the tip of the instrument should not be carried too deep into the underlying tissue since there is grave danger of producing a stricture. While large scale cauterization is being done the cervical canal should be periodically dilated to preclude stricture while healing takes place. If the patient is under 35 years and the lesion does not bleed one might well omit a biopsy. One must ever be on guard for portions of the lesion that do not heal promptly, six weeks being the average healing time. Even in the young, carcinoma of the cervix does occur. It is conceivable that a malignancy might well be present with the erosion. Nonhealing of a cauterized point is an absolute indication for biopsy to rule out cancer.

Instead of cauterizing the cervix, conization is often resorted to in young women. This we feel is contraindicated in women below the age of 40 since the incidence of stricture is high. The incidence of cervical dystocia in patients who have been conized is not insignificant. We have encountered one where cearean section had to be done within two years after a radical conization had been performed. Hyam,<sup>3</sup> Sackett<sup>4</sup> and Schwartz<sup>5</sup> warn us on this very detail. Miller and Todd<sup>6</sup> advise against this minor operation in the reproductive years for other reasons, and state that there is no substitute for the cautery. With this I fully agree.

*Bartholin Gland*—Recurrent (chronic) Bartholin abscess is a common-place lower genital tract lesion. The vulvovaginal gland will flare up and rupture at rather regular intervals unless it is surgically excised. An enthusiastic surgeon might be tempted to try surgical removal of this gland in his office, as a purely local procedure. One would probably not attempt this more than once, since the gland bed is so rich in blood supply that deep mattress sutures are required for hemostasis. A well equipped operating room and good anesthesia are necessary for this minor operation. The operation per se is not difficult: an incision is made along the mucocutaneous border just over the gland. Sharp dissection around the capsule, whether it breaks or not, and dissection of the entire lining constitute the essentials of technique. Very fine catgut mattress and interrupted suture repair will control bleeding and approximate the skin edges. No drain is necessary.

*Upper Genital Tract.*—Since acute gonorrheal endometritis is a self-limiting disease we need have little concern for recurrent or chronic endometritis. In years past this was rather a common diagnosis by clinician and pathologist alike; however, better understanding of endometrial changes have shown that chronic endometritis is rarely if ever the correct diagnosis in any given case. It will be recalled that gonorrhea travels to the tube by way of the endometrial canal and during this very short interval the uterine canal will show inflammatory change. The gonococcus has a preference for the salpinges and to a lesser extent the

ovaries and surrounding peritoneum. The adnexa are our chief concern in upper genital recurrent infection.

The gross pathologic picture of old minimal gonorrhea involving the adnexa is a tube slightly larger than normal, fimbria firmly closed, with both the tube and ovary bound together or separately being adherent to the posterior leaf of the broad ligament. This lesion is as a rule asymptomatic and requires no surgery. However, such a lesion is a cause of mechanical sterility and as such is quite amenable to surgical correction (Obviously it would be unwise to operate upon such a patient with a hope of correcting infertility if the husband has azoospermia)



Fig. 408 —Fimbria held open, thumb forceps in the lumen of tube and sulfanilamide crystals poured in

The technic that has given the best results has been described by Beecham and Sigman.<sup>7</sup> It is not only feasible for the correction of tubal block but for other manifestations of upper tract gonorrhea. In brief, this technic consists of a salpingolysis and lysis of adhesions about the ovary. With the adnexa free the fimbriated end of the tube is held up with visceral forceps and the closed ostium cut open with a scalpel. The tube is next gently dilated with a long, narrow hemostat. Then with a long thumb forcep in the lumen of the tube as close to the isthmus as it will easily go, the prongs are allowed to separate and 5 gm. of sulfanilamide crystals are poured into the lumen while the excess spills over the pelvis (Fig. 408). The abdomen is of course closed without drainage.

Where tubal block is due to this type of pathology, we find that 90 per cent of the tubes remain patent after operation and between 30 and 40 per cent of the patients conceive. No ectopic pregnancies have been observed following the employment of this technic.

The operation of salpingolysis and sulfanilamide implantation is applicable for large, thick, dilated tubes up to 3 cm. in diameter. Beyond that point in size we have not used this procedure. The ovaries in these cases are usually twice their normal size, being filled with follicular cysts and usually densely adherent. Since these ovarian enlargements are non-neoplastic they need not be removed.

Falk<sup>8, 9, 10</sup> has described a conservative operation for these oft recurrent cases of inflammatory disease that deserves careful consideration by every gynecologist. The clinical course of recurrent gonorrhea is a rough one. The remissions and exacerbations are well known to all, with their resultant crippling pain and menorrhagia. Falk feels that these recurrent cases are reinfected along the same route (*endometrium*) as in the initial infection and that the bacterial agents are mixed in type. Therefore Falk does a bilateral cornual resection to interrupt the bacteria in their journey from the lower genital tract to the upper tract. The adnexa are left alone in most cases regardless of how serious or destructive the infection has been. In a large series and for several years Falk has followed this conservative principle and his published results with only 1.5 per cent failures are superior to those obtained by more radical steps.

We have employed the cornual resection for several years and find that on the average our results are good although not up to those reported by Falk. Our residents have on occasions employed this technic of cornual resection where more mature operators would have removed the adnexa as with a ruptured tubo-ovarian abscess. We have found that such a major lesion heals with an uneventful postoperative course and the patients are free of complaints. The pelvis demonstrates little, if any palpable disease. At this writing, I believe that as we gain more experience in the employment of Falk's procedure we will remove very few adnexa for inflammatory disease.

### PELVIC CELLULITIS

Gonorrhea may be described as a crippling disease quite in contrast to cellulitis, which is a serious threat to life. Over the past few years much help has come our way in the form of chemotherapy and antibiotics, yet cellulitis continues to kill people. As a rule this type of infection is mixed but the anaerobes are usually present and are untouched by our new therapeutic agents. The incidence of cellulitis would

seem to remain unchanged, or possibly we see more today or perhaps recognize more, than in years gone by.

**Causes and Site of Infection.**—The principal causes of pelvic cellulitis are *induced abortion, puerperal trauma, instrumentation of cervix and/or corpus uteri*. Thus the infection is in the upper genital tract, starting in the uterus and spreading from the placental site or point of uterine trauma. The lymphatics and blood stream carry the infection through the uterine wall into the parametrium and broad ligament. The veins of the broad ligament develop extensive thrombophlebitis that frequently involves lateral channels and may extend into the lower extremities. There is certainly extension along the endometrium into the tube although we do not see the usual picture of endosalpingitis but rather a perisalpingitis. In cellulitis, perisalpingitis overshadows the endosalpingitis. The ovary is most frequently involved in such an infection and ovarian abscesses are quite common. Peritonitis is usually present and demands careful observation and care. With the vast ramification of possibilities in this serious disease it is apparent why cellulitis is a serious threat to life.

At the onset of cellulitis there is no indication for surgery. Before therapy is begun, a gentle but thorough pelvic examination should be done and intrauterine cultures taken. The majority of cases are septic abortions with puerperal sepsis being the next most frequent entity. Let us consider septic abortion.

**Septic Abortion.**—At the initial examination of an infected abortion, the cervix is usually dilated or at least patulous. Placental fragments may be seen in the os and if so they should be gently teased out. Forceful attempt at digital manipulation should not be carried out. Intrauterine cultures should be taken unless the patient is bleeding profusely. If there is a *life-threatening hemorrhage* present the patient should be taken to the operating room and an evacuation gently done with a placental forcep and a dull curette. We are not in accord with those who state that all incomplete abortions (which includes the septic cases) should be evacuated immediately. Experience in Philadelphia, where all maternal deaths are reported and investigated by the County Medical Society, has definitely shown intrauterine manipulation of a septic case to be hazardous and often lethal. There is only one exception—*life-threatening hemorrhage*.

**Treatment.**—The extremely ill patient (not infrequently from severe peritonitis) is first given one million units of penicillin intravenously on admission. Sulfanamide therapy is frequently added along with intense supportive treatment that should include blood transfusions. Daily doses of penicillin should be maintained at a high level, at least 600,000



## MODERN INDICATIONS FOR CESAREAN SECTION

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MEDICINE is a mixture of art and science. When mathematics can be applied to all the factors in a special field of knowledge, it may be classed as a precision field of science. Because of the variations in humans it is impossible to treat patients according to mathematical principles only, hence the modern indications for cesarean section are based on the knowledge acquired from the newer methods of measuring the various factors of disease. The application of this knowledge is still an art.

### EVALUATION OF THE OPERATIVE RISK

The chief dangers of cesarean section are hemorrhage and infection, specifically peritonitis. These dangers have been controlled by improved surgical technics, modern anesthetics, blood transfusion, sulfonamides, antibiotics and oxytocics, so that the risk of cesarean section has been reduced to that of vaginal delivery of a few decades ago. Now that cesarean section may be used with greater impunity, the indications have been broadened to include many conditions that formerly were forbidden because of the great risk. This means saving from death or damage of more mothers and babies. However, a new risk has been added. Due to a false sense of security on the part of the obstetrician, cesarean section may be abused by substituting it for a less risky delivery through the birth canal. True, a vaginal delivery may require more patience and skill, but to prevent such abuse the physician must be able to evaluate and balance the risks of various procedures and have the skill to carry each procedure to a successful conclusion. There is no place in obstetrics for the "one operation" obstetrician. While the "obstetric cripple," suffering from the effects of a mismanaged or poorly advised vaginal delivery, is a distressing sight, it must not be forgotten, in the desire to prevent such an unfortunate result, that there is the "cesarean cripple." If there is a breakdown of any of the factors of safety, such as surgical skill and judgment, operating room technic or anesthesia, death or permanent injury to mother or baby will follow. It must not be forgotten that the risk in cesarean section is five to ten times greater than in vaginal deliveries. The most favorable figures will show a maternal

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mortality for cesarean section of 0.5 to 1 per cent, but for normal vaginal delivery a mortality rate of less than 0.1 per cent at similar clinics

Dystocia, hemorrhage and similar major complications offer the chief indications for cesarean section, which should be decided on the following evaluation of risks

1 If the danger to mother or child by vaginal delivery is less, cesarean section is contraindicated

2. If the danger to mother or child by vaginal delivery is equal to cesarean section, then the type of delivery selected will depend on the skill of the obstetrician. Some of the problems of this group are now included in the modern indications for cesarean section where formerly vaginal delivery was indicated.

3 If the danger to mother or child is greater by vaginal delivery than cesarean section is indicated

### CONSIDERATION OF INDICATIONS

**Inlet Contractions.**—Fetal-pelvic disproportion at the inlet may be recognized before the onset of labor by the physical signs of abnormal presentation, high presenting part, premature rupture of the membranes and pelvic mensuration. The knowledge of pelvic mensuration has been advanced greatly by roentgen pelvimetry and cephalometry as developed by the studies of Caldwell, Moloy and D'Esopo<sup>1</sup> and those of Thoms.<sup>2</sup> The following criteria should be used in evaluation of contracted pelvis with disproportion at the inlet

- 1 Shape of the inlet
- 2 Anteroposterior diameter (true conjugate)
- 3 Transverse diameter
- 4 Size of the fetus, particularly the head.

The *shape of the pelvic inlet* is of great importance. Android and anthropoid pelvis, when contracted, offer greater obstruction than gynecoid and flat pelvis contracted to the same degree, chiefly because of deficient space laterally due either to the straight side walls of the android combined with its short posterior segment or the short transverse diameter of the anthropoid.

The *anteroposterior diameter or true conjugate* is still the most dependable measurement available in recognizing contracted pelvis by physical examination. The usual standards for deciding the management are: (1) True conjugate above 9.5 cm.—probable delivery through the birth canal (2) True conjugate between 7 cm. and 9.5 cm. (borderline group)—test of labor with some prospects of vaginal delivery (3) True conjugate 7 cm. or less—cesarean section.

However, the newer knowledge obtained by roentgen examination has

shown that these standards are not accurate enough and, in addition to pelvic shape and true conjugate, many other dimensions should be measured. One of the most valuable is the *transverse diameter* of the inlet. When this is shorter than 12 cm. it is definitely contracted and if a shortened true conjugate is also present a cesarean section is usually indicated even if the true conjugate is only moderately shortened. A true conjugate of 9.5 cm. usually will permit the passage of a normal baby through the inlet, but if the transverse diameter is 11.5 cm. and the fetus the same size, the pelvis usually is too small for vaginal delivery.



Fig 409.—Abbfeld's method for measuring the growth of the fetus. Each lunar month equals 3 cm., and full term average baby is about 30 cm.

The *size of the fetus* is a factor which must always be considered, together with the degree of molding which may occur. Roentgen cephalometry has made great strides in measuring the fetal skull but falls short of complete accuracy. In cephalic presentations it is useful because the head is fixed in a measurable portion of the pelvis, but in breech and transverse presentations it cannot be measured adequately enough to give dependable results. Palpation and abdominal mensuration are still valuable procedures (Figs 409, 410, 411). Likewise, present methods cannot estimate the degree of molding that may be permitted without causing intracranial damage. True, premature babies mold more easily and are more delicate than mature and postmature ones, but this cri-



Fig 410 — MacDonald's method for measuring the growth of the fetus. Each lunar month equals 3.3 cm, and full term average sized baby equals about 33 cm (33 cm to 37 cm).



Fig 411 — Method of estimating the size of the fetal skull. Two centimeters are subtracted for the thickness of the abdominal wall. This is an inaccurate method and the results should be noted only as large, medium or small. It is of some value in breech presentations.

terion is not safe enough to be dependable in making a sure prediction as to the course of labor in the case of contracted pelvis.

The study of the problem of labor in a contracted pelvis thus depends on the evaluation of that particular baby in that particular pelvis, and

such a study should be made by the obstetrician. Dependence on an x-ray report alone will lead only to disaster, sooner or later, or to unnecessary cesarean sections. It is not fair to a roentgenologist to have the responsibility of making an important clinical decision by measuring a film. The obstetrician should consider all the available data but depend most of all on careful physical examination and observation of the patient. It is his responsibility and his alone to make the final decision as to the management of the case.

An example of a large pelvis requiring cesarean section is seen in Case I.

CASE I.—K. H. (Hosp No. 7648), aged 28, a short, fat gravida II, was admitted to Hahnemann Hospital after twelve hours of unsuccessful labor in another hospital. Two years previously she had delivered normally of a baby

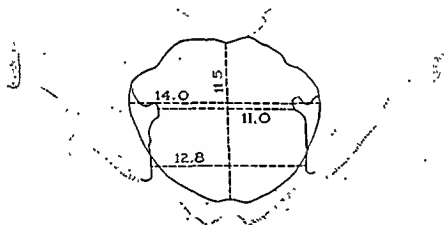


Fig. 412 (Case I) —A normal gynecoid pelvis requiring delivery by cesarean section after twenty-two hours of labor because of a very large baby. Tracing from x-ray film.

weighing 3147 gm. (6 pounds, 15 ounces). Her height was 1.54 m. (5 ft.) and weight 134 kg. (295 pounds). Pelvic measurements were all large (Fig. 412) and labor pains seemed weak. With a diagnosis of primary inertia the patient was treated by sedation and careful observation. Complete dilatation was reached ten hours after admission, or a total of twenty-two hours of labor. Vaginal examination showed L.O.T. position with some posterior asynclitism and head at "station +2". At this time the membranes were ruptured.

Because of the presence of beginning fatigue the patient was anesthetized and application of Kielland forceps was attempted and failed. The Chief was called and Barton forceps were applied easily, but on the first effort of traction the head failed to descend. Re-examination showed that the head was at "station -2" and could not be brought below "station -1"; in other words, cephalopelvic disproportion was present. The patient was taken to the operating room and an immediate Norton extraperitoneal cesarean section done. The baby was

large, weighing 5440 gm (11 pounds, 12 ounces) with a biparietal diameter of 10 cm, a suboccipitobregmatic diameter of 11 cm and occipitomenal diameter of 15 cm. Marked molding was present showing that the uterine contractions were stronger than originally diagnosed and that the cephalo-pelvic disproportion was the important factor in the dystocia. With the aid of antibiotics convalescence was complicated only by superficial wound infection and mother and baby were discharged in good condition on the seventeenth day postpartum.

Had the pelvimetry and the history of a previous spontaneous delivery of a normal full term baby been the only factors in deciding the management of the case the ultimate outcome would have been an obstetrical disaster; for this particular child in this particular pelvis required cesarean section.

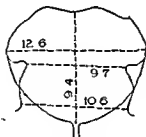


Fig. 413 (Case II).—A gynecoplatypelloid pelvis shortened in all directions yet a small fetus delivered through it normally. Tracing from x-ray film.

**CASE II**—A B (Hosp No 12056), aged 28 years, a primigravida, was easily identified in the prenatal clinic as having a flat rachitic pelvis. Roentgen pelvimetry (Fig 413) showed small measurements, both of the true conjugate and transverse diameter of the inlet. Since she was in the moderate disproportion group a test of labor was selected as the best treatment for her. She delivered spontaneously after thirteen and a half hours of normal labor under close observation. The baby weighed 3161 gm (6 pounds, 15½ ounces), with a biparietal diameter of 8.5 cm and a suboccipitobregmatic diameter of 8.5 cm.

This case illustrates a small pelvis with spontaneous delivery. This particular baby in this particular pelvis had no labor trouble but this does not guarantee what will happen in future labors.

**The Müller-Hillis Maneuver**—The best method of individualizing fetus and pelvis by physical examination was first described by Müller<sup>3</sup> and later improved by Hillis,<sup>4</sup> and consists of placing a finger in the rectum or vagina while the other hand (or an assistant) presses on the fundus (Fig 414). In this way the head is brought down to engagement, or below, if there is no disproportion. If disproportion is present it can-

not be engaged. (Engagement<sup>6</sup> is defined as being present when the head covers three-fourths of the symphysis pubes, two-thirds of the sacrum and the most dependent portion of the skull, not scalp, reaches an imaginary line drawn between the ischial spines. This is known as "station 0.") In flat pelvis the head must descend 1 cm. lower before it is engaged.

The chief sources of error in the Müller-Hillis maneuver are, first, the presence of an undeveloped lower uterine segment which may keep the fetal head high and is associated with a thick cervix. Second, the

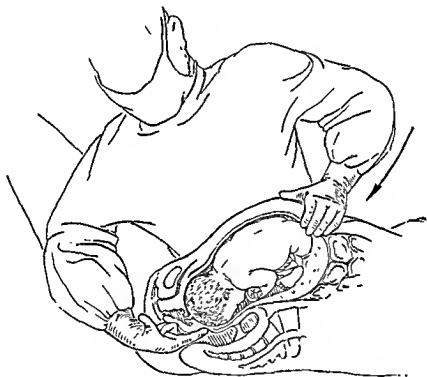


Fig 414.—Müller-Hillis maneuver for determining whether the head can be engaged. (Modified from DeLee-Greenhill)

inexperienced observer often estimates the head as being lower than it actually is, as shown in Case I. Another criticism is that it is useful in cephalic presentations only. Nevertheless, this is one of the most useful tests that can be done and should be applied to every pregnant woman shortly before term.

When disproportion at the inlet has been discovered during pregnancy, by physical signs and pelvimetry, then complete roentgen studies should be made and the case evaluated. If disproportion is extreme, elective cesarean section should be selected; if moderate, the patient should

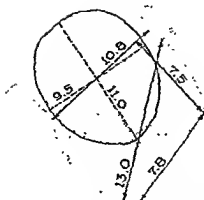


Fig 415 — Full term pregnancy in a normal pelvis. Note that the head is engaged before the onset of labor. The most dependent portion of the skull has reached the ischial spines, "station 0", and three fourths of the symphysis pubis and two thirds of the sacrum are covered by the fetal head. Tracing from x-ray film.

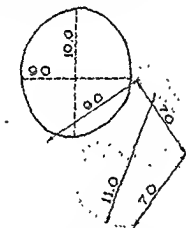


Fig 416 — An example of disproportion before the onset of labor. The head is unengaged at "station -4" or 4 cm. above the ischial spines. This patient showed a platypelvi-android inlet with overriding of the fetal head. A six hour test of labor failed and a living baby weighing 2863 gm (6 pounds, 5 ounces) was delivered by extraperitoneal cesarean section. Tracing from x-ray film.

be given a test of labor. A satisfactory method of evaluating the degree of disproportion is found again in the Müller-Hillis maneuver and the author uses the following standards:

1. Severe disproportion exists if, in the presence of a well developed lower uterine segment, the head cannot be brought lower than 3 cm. short of engagement (station -3). An elective cesarean section is in-

dicated and other common signs of disproportion usually are present.

2. Moderate disproportion exists if the head can be brought lower than 3 cm. short of engagement but still does not engage (between "station -3" and "station 0"). A test of labor is then indicated. It is in this group that disproportion is often missed, particularly if the head can be brought down to "station -1". Too often it is interpreted as reaching "station 0" or even "+1" where a little more care and skill in making the examination would show the true condition.

*Test of Labor.*—At present there is no clearly defined test of labor, other than the well-known anatomicphysiologic test and this is usually too prolonged to be considered safe; a proper decision can be made long before such a severe test is completed. The most important factors involved in a test of labor are:

1. The shape and size of the pelvis.
2. The size of the baby and degree of molding.
3. The strength and frequency of uterine contractions.

These factors involve so many variables that there are no standards used other than an arbitrary number of hours selected by each individual obstetrician. The impatient and the surgically minded prefer a short time and the more patient and conservative ones, a longer time.

I have attempted to solve this problem by using the following standards. After labor is established, with a good uterine contraction lasting longer than thirty seconds, at five minute intervals or oftener, and showing some shortening and effacement of the cervix, a Müller-Hillis maneuver is done every three or four hours. The shorter interval is used when the labor is more active and the longer, if less. If the test is going to succeed it will be found that at each maneuver the head can be brought to a slightly lower level and the test may be continued. However, if at the second of two successive maneuvers progress is stationary and the head cannot be brought to a lower level than at the previous examination, the test should be considered a failure and the baby delivered by cesarean section without further delay. Thus, a decision can be reached before the complete dilatation and two hours of labor required by the anatomicphysiologic test. In fact, the success of the test is dependent on the fact that in normal labor the head will descend through the pelvic inlet before the cervix is fully dilated.

This test is far from perfect because there are still variable factors that cannot be calculated, but it does prevent unnecessary cesarean section from faulty judgment and lack of careful observation. Likewise, the ease of true obstruction will be recognized long before exhaustion and serious danger of infection are present. The errors most commonly observed are the tendency to estimate the head as being lower in the



pelvis than it actually is and to mistake caput succedaneum for the most dependent portion of the skull. If there is any question in the physician's mind as to the success of the test it is best not to consider the test satisfactory until the head reaches 1 cm. below the ischial spines ("station +1").

**Midpelvis Contraction.**—Contraction of the midpelvis is occasionally seen, usually in android and anthropoid pelvises (Fig. 417), and is first recognized during the physical examination by the prominence of the ischial spines. As soon as this is discovered the sacrosciatic notch should be palpated and its width in fingerbreadths noted (Fig. 418). This maneuver gives an excellent idea of the length of the posterior sagittal

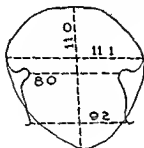


Fig. 417 —Contraction of the midpelvis in an anthropoid-android pelvis. At labor the baby presented as R O P, developed into persistent occiput posterior with arrest at midpelvis, requiring a difficult forceps delivery. The baby weighed 3000 gm (6 pounds, 13 ounces), showed excessive molding, but was living and healthy. Roentgen pelvimetry was done postpartum to explain the unexpected dystocia, since prenatal pelvimetry was classed as "normal." Had the roentgen pelvimetry been done antepartum an elective cesarean section would have been chosen. Tracing from x-ray film.

diameter at the midplane or plane of least dimensions. Moloy<sup>6</sup> states the minimum normal as 2 fingerbreadths. Two and a half is usual and 3 not uncommon. The patient should then have roentgen pelvimetry. If the interschial diameter is less than 9 cm. and the posterior segment is short, owing to the shallow curve of the sacrum, cesarean section is usually indicated.

A test of labor may be permitted in midplane contraction since the head is not too low at this level to be reached by abdominal section. Such tests should not last a long time but if progress is definitely arrested at the ischial spines cesarean section should follow promptly.

**Outlet Contractions.**—A contracted outlet, severe enough to require cesarean section, is quite rare but must be recognized early. Once the

descending head has reached the narrow outlet and obstruction develops, a destructive operation is the proper treatment; for with the narrow intertuberos transverse diameter and the short posterior segment due to the shallow sacrum, the baby will be badly damaged or killed if forceps are attempted. The rule of "fifteen" still holds true in the management of these cases; that is, if the total length of the intertuberos and the posterior sagittal diameters add up to 15 cm. or more there is room for delivery through the outlet, but if the total of these two measurements is less than 15 cm. an elective cesarean section is indicated.



Fig. 418.—Maneuver for estimating the width of the sacrospinous notch. This gives information as to the length of the posterior sagittal diameter at the plane of least pelvic dimensions and assists in evaluating the pelvic outlet. Two and a half fingers is average, two fingers the minimum normal and three fingers large. It may be determined by either vaginal or rectal palpation.

**Soft Tissue Obstruction.**—Stenosis of the cervix usually requires cesarean section and is commonly acquired rather than congenital. It follows one of the varieties of surgical treatment to the cervix, since any procedure that leads to production of extensive scar tissue will cause rigidity. Application of radium to the cervical canal produces a hard, rigid scar, as does deep cauterization with the thermocautery. Should women in this category conceive, an elective cesarean section is always indicated. Extensive trachelorrhaphy for deep tears may cause a rigid cervix, particularly if the wound developed postoperative infection.

On the other hand, conization of the cervix, either radical and deep,

or superficial, will not interfere with future labors, neither will superficial cauterization, nor will amputation of the cervix or short trachelorrhaphies that heal by first intention. Patients who have been subjected to these procedures should all be permitted to deliver normally unless there is some other indication for cesarean section. Trachelorrhaphies often will tear along the line of the old scar at succeeding deliveries but these tears may be repaired immediately at the time of delivery, with perfect wound healing. These facts should be kept in mind when treating a diseased cervix in a young woman. Conization or amputation should be used whenever possible and future unnecessary cesarean sections will be avoided.

Again the same problem is present by pregnancy following vaginal plastic operation. The vagina maybe so rigid as to cause serious obstruction or else serious tears may accompany delivery. If a large cystocele has been repaired and the probability is that the next labor will injure the new bladder floor, vaginal delivery should not risked, for the bladder fascia cannot be protected as adequately by episiotomy as the rectal fascia can. If the vaginal plastic was only a perineorrhaphy, cesarean section is unnecessary.

These facts are true following operations for retroflexion and prolapse. In general, where repair surgery has been extensive and elaborate, elective cesarean section is the procedure of choice, but this statement should not be interpreted as meaning cesarean section is to be used following all repair operations. If a careful selection is made of patients and choice of operation, a skillful obstetrician may carry such a case successfully through a succeeding delivery. In these cases it is advisable always to use a wide episiotomy and to inspect and repair the cervix immediately following delivery.

**Tumors.**—Ovarian cysts and pedunculated fibroids are best removed at about the end of the fourth lunar month of pregnancy, if they are of any size, small ones may be left alone. If the patient reached term and a tumor takes up enough space in the pelvic inlet to cause dystocia, the patient should be delivered by cesarean section. Tumors higher in the abdomen, near the fundus, should not interfere with labor. At the time of section myomectomy may be performed if the tumor is easily removable, but the patient should not be subjected to long and elaborate surgery during a cesarean section until conditions are safer. Carcinoma of the cervix is rare but, if discovered, the fetus should not be permitted to pass through the cervical canal but should be delivered by cesarean section, either classic or cesarean hysterectomy according to the treatment has been reduced to that of vaginal delivery of a few decades ago. ment planned for the carcinoma.

Congenital anomalies require cesarean section whenever they cause stenosis and obstruction, otherwise they do not interfere with labor. One that should be watched is the double uterus. If the nonpregnant uterus becomes incarcerated in front of the fetus, it will act the same as a blocking tumor and cesarean section is indicated.

**Spastic Contraction Rings.**—Since spastic contraction rings can be diagnosed positively only by a hand in the uterus, they are not often recognized. Most of such manifestations of local tetany respond to anti-spasmodics such as demerol and scopolamine in combination, but if a permanent constriction ring is present only cesarean section will deliver the baby. I once performed an extraperitoneal cesarean section for an impacted transverse presentation and after the uterus was incised in the lower segment a permanent constriction ring was found above the incision at the junction of the lower and upper segments. The baby could be delivered only by opening the peritoneum and extending the incision upward through the ring. Both baby and mother recovered uneventfully with the aid of antibiotics. These spastic constriction rings are not to be confused with the retraction ring of Bandl.

**Hemorrhage.**—*Placenta praecia* and *premature separation of the placenta* have much in common as far as indications for cesarean section are concerned. The two chief points for consideration are the amount of bleeding and the degree of cervical dilatation. Active bleeding requires prompt treatment and the quickest way to control such hemorrhage is to deliver the baby and placenta. If the cervix is incompletely dilated, preliminary operations to complete dilatation only add further trauma and hemorrhage, making a bad case worse. Cesarean section solves the problem quickly and efficiently. If the bleeding is only slight, more conservative measures may be used; or if the cervix is fully dilated, forceps or even version are indicated. The big danger in hemorrhage cases is active bleeding in the presence of an incompletely dilated cervix, and in such a situation cesarean section should be the first treatment considered.

While in *placenta praecia* cesarean section is usually indicated in the *centralis* and *partialis* varieties, the *marginal* type may be treated by more conservative methods, such as puncture of membranes, Braxton-Hicks version, Willett's traction forceps and others. In *premature separation*, particularly *abruptio placentae*, with a long cervix, cesarean section is to be chosen. In the milder types the accepted conservative methods may be used, especially if the baby is dead, but if there is a chance to obtain a living child cesarean section offers the best hope and the burden of proof of correct judgment lies on him who decides otherwise.

**Toxemia.**—At one time cesarean section was offered as a treatment

for pre-eclampsia and eclampsia but the results were so disastrous that it has been discarded in all modern clinics. Occasionally certain rare cases of pre-eclampsia which are changing rapidly from bad to worse, in spite of skillful treatment, are entitled to prompt cesarean section, particularly where the cervix is long and thick with the prospect of failure by medical-surgical induction. With the development of the newer technics for the prevention and treatment of pre-eclampsia it is likely that soon toxemia per se will cease to be an indication for cesarean section. Of course, the presence with toxemia of other obstetrical indications such as disproportion, dystocia and hemorrhage is a different matter and these will require cesarean section on their own merits, in fact risking a long difficult labor in the presence of toxemia only increases the hazard. Fortunately such cases are rare, for the fetus in toxemia is small and disproportion is seldom encountered.

**Heart Disease.**—If the amount of work done by the heart during labor could be calculated in ergs the problem of heart disease combined with pregnancy would be simple: select the method which requires the least work. Formerly it was thought that cesarean section put less strain on the heart than labor but since the important work of Hamilton<sup>7</sup> at the Boston Lying-in Hospital and others the following standard is the accepted criterion:

1. Normal labor with late first stage analgesia and outlet forceps offers the least amount of heart load.

2. Cesarean section puts a greater strain on the heart.

3. Dystocia puts the greatest strain on the heart.

Therefore, cesarean section is indicated in heart disease only when there is a prospect of obstruction due to disproportion or to dystocia from other causes.

**Other Maternal Diseases.**—In general, the disease should be treated first, the pregnancy given second consideration. Cesarean section is not indicated except for strictly obstetrical reasons. Labor in thyrotoxicosis and pulmonary tuberculosis should be treated on the same principles as heart disease. Diabetes may require cesarean section in those cases in which the chorionic gonadotropin levels persist above normal, in spite of adequate estrogen and progestin therapy, with the consequent danger of an oversize, over-term, dead fetus. Here an elective cesarean section is indicated about two weeks before the calculated date, provided palpation and abdominal mensuration show the fetus is large enough to be viable.

*Sterilization per se* is not an indication for cesarean section.

**Fetal Indications.**—Abnormal presentation and position is one of the

signs of pelvic inlet contraction before the onset of labor, as stated earlier; but this does not mean that disproportion is the only cause. In general, abnormal presentation in a contracted pelvis is an indication for cesarean section, but when the contraction is only slight and the fetus small, vaginal delivery is the better choice. Transverse presentations are particularly dangerous and a primigravida with dry labor should be sectioned even if the pelvis is normal. Multiparas with normal pelvis and ruptured membranes should be treated conservatively as long as dilatation proceeds rapidly and there is enough amniotic fluid to turn the baby.

Breech presentations in a primigravida should be studied carefully; if the pelvis is contracted more than a slight degree, elective cesarean section is indicated. Elderly primigravida approaching 40 years of age should be treated the same way even if the pelvis is normal since the baby has a high priority, and it is impossible to predict how the after-coming head will descend through the pelvis. Of course greater pelvic contractions require cesarean section unless it has been proved that a large sized baby can be delivered safely through the birth canal by previous successful labors; for there is no way of conducting a test of labor in either breech or transverse presentations. The correct decision must be made, at the latest, before the first stage is completed.

Fetal monsters commonly present abnormally and can be recognized in most instances by roentgen studies. The most treacherous cases are hydrocephalus with breech presentation and soft tissue tumors that do not cast a shadow on x-ray film. In general, monsters are not an indication for cesarean section but should be treated by destructive operation after the cervix is fully dilated. Rarely cesarean section must be done when a vaginal delivery is impossible.

Marked variation of the fetal heart rate during labor is one of the newer indications for cesarean section and this indication should be used with caution. It is usually a sign of cord complications, such as forelying cord, occult prolapse of the cord, tight loops and coils of a long cord or an unduly short cord. This is not an indication for cesarean section before the onset of labor unless the fetal heart rate shows very marked change of rate. The best example of such indication is seen in a primigravida with very little cervical dilatation and marked variations of the fetal heart rate between pains. The normal slowing of the fetal heart rate during uterine contractions is not included in this category.

The elderly primigravida of 40 years or over usually should be delivered by elective cesarean section because of the high priority value of the baby. In most cases this is the woman's only chance to have a

baby and with the difficulties of labor likely to be encountered it is best to offer the fetus every opportunity for safe delivery. Again this is a generalization and there are occasional exceptions, for each case should be decided on its own merits.

Last of all, cesarean section in a dying mother or immediately post-mortem is a fetal indication that should not be forgotten.

**Repeated Cesarean Section.**—The dictum of "once a cesarean section always a cesarean section" is not necessarily true, for with careful study, observation and skill certain patients who previously had cesarean section may be delivered successfully through the birth canal. Elective cesarean section is required in all cases in which the previous indication was contracted pelvis, likewise if wound healing at the former section was complicated by endometritis and uterine infection, since there is danger of rupture of the uterine scar during the next labor. In other words, cesarean section is indicated in a succeeding labor if there is danger of obstruction, dystocia or rupture of the uterine scar due to poor wound healing. Delivery through the vagina may be considered and attempted if the previous section was for hemorrhage, toxemia or similar indication where the problem of dystocia was not involved and convalescence was uncomplicated by infection.

In addition, there should be the prospect of an easy delivery at the coming labor; cephalic presentation, normal pelvis and plenty of room for that particular fetus are all necessary conditions. Of course, labor in these cases should be conducted in a hospital equipped to provide immediate operating room service at any time of the day or night and the obstetrician must be in continuous attendance. The labor is managed the same as in a case of heart disease, analgesia for the first stage and forceps for the perineal stage. If obstruction or any other abnormal signs occur, immediate surgical delivery is indicated according to the conditions present, preferably cesarean section if the cervix is not completely dilated.

**CASE III**—Mrs. R. T. was delivered by the author in 1925, 1926 and 1928. The labors were easy and normal, the babies weighed between 3000 gm (6 pounds, 10 ounces) and 3289 gm (7 pounds, 4 ounces). The fourth pregnancy was complicated by placenta praevia partialis which appeared at the thirty-sixth week of pregnancy and was treated by classic cesarean section with normal convalescence. The baby weighed 1941 gm (4 pounds, 8 ounces) and grew nicely. Following this episode there were three more pregnancies with easy deliveries in 1935, 1937 and 1941, the last one complicated by a uterine myofibroma. These three babies were small and weighed between 2635 gm (5 pounds, 14 ounces) and 3080 gm (6 pounds, 14 ounces). The myofibroma grew rapidly

to about 20 cm in diameter and it was excised by hysterectomy six months later. Microscopic examination of the old cesarean scar showed perfect wound healing with interlacing muscle bundles and no thinning of the uterine wall.

**CASE IV.**—Mrs. R. B (Hosp. No 12158), aged 19 years, developed severe pre-eclampsia during her first pregnancy and became worse in spite of careful conservative treatment so that pregnancy was terminated at thirty weeks by classic cesarean section. The living premature baby weighed 1588 gm. (3 pounds, 8 ounces) and the mother's convalescence was normal. Six months later she became pregnant again and was carried to term under careful prenatal care and delivered normally, with demerol, scopolamine, perineal block and episiotomy, of a healthy baby weighing 2805 gm. (6 pounds, 4 ounces). The labor lasted eighteen hours but the uterine contractions were never severe at any time.

### TYPES OF CESAREAN SECTION

**Extraperitoneal Operation.**—The work of Waters<sup>8</sup> and Norton<sup>9</sup> have developed the technic of this operation to the point where it is simple enough and safe enough to be required as part of the armamentarium of every qualified obstetrician. The most important requirement is a well developed lower uterine segment long enough to permit an adequate incision for delivery of the fetus. This condition is present only at term, just before the onset of labor, or during labor. In fact, labor causes a thinning out of the lower uterine segment which makes the fascial planes, bladder and peritoneal fold more easily identified consequently this is an operation for full term intrapartum or antepartum cases.

The chief advantages are diminished danger of peritonitis and diminished danger of rupture of the uterine scar at succeeding pregnancies. The disadvantages are the inaccessibility to the abdominal cavity for sterilization and the danger of bladder injury. The latter can be overcome by prompt repair at the time of injury and by practice for no greater skill is necessary for this operation than is needed for an anterior colporrhaphy; only the unfamiliar anatomy presents a hazard.

The best indication for this operation is an infected labor requiring cesarean section, as the peritoneal cavity is not opened and the risk of peritonitis is reduced to that of forceps or version. The value of extraperitoneal cesarean section in these cases is not fully accepted as yet and some excellent authorities believe that cesarean hysterectomy offers greater safety. In order to throw light on this question McCall<sup>10</sup> analyzed a series of cases in which the extraperitoneal operation was done by him, Briscoe, and the author and that exceeded Dieckman's criteria<sup>11</sup> for an infected labor requiring cesarean hysterectomy.



Dieckman's criteria\* for the extraperitoneal operation are.

1. Labor over twenty-four hours.
2. Ruptured membranes over twenty-four hours
3. Attempts at delivery by forceps or version.
4. Induction of labor by bag bougie or pack
5. Evidence of uterine infection
6. More than six vaginal examinations.
7. More than twelve rectal examinations
8. Dead or damaged fetus.

There were sixty-four cases in the series with no maternal deaths and eight fetal deaths, suggesting that extraperitoneal cesarean section is an excellent method of handling this problem.

This operation is equally well indicated in "clean" cases where a test of labor has failed and it may be used as an elective operation before the onset of labor provided the lower uterine segment is well developed. It is contraindicated in prematurity, distortion of the anatomy by adhesions or uterine tumors and when speed is important, although Waters, Norton and others have developed their skill to such a degree that the operation may be performed as quickly as a classic cesarean section.

**Low Cervical Operation.**—This operation is now fully established and is a marked improvement over the classic cesarean section. Like the extraperitoneal section a fully developed lower uterine segment must be present as a required condition. Its advantages are greater protection from peritonitis than the classic operation accessibility to the peritoneal cavity for other surgical procedures such as sterilization or exact internal pelvimetry and less danger of rupture of the uterine scar in succeeding pregnancies and labors than in the classic section. The disadvantages are greater danger of peritonitis than with extraperitoneal section and greater technical difficulty than with classic section. Low cervical section is indicated in elective cesarean section at term, particularly if sterilization is planned, and after an unsuccessful test of labor that has been conducted under strict aseptic precautions, especially for those obstetricians who have not acquired proficiency in the extraperitoneal operation. It is contraindicated in premature delivery and infected

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\*Since this article was submitted to the editors for publication Dieckman<sup>11</sup> has modified the criteria for cesarean hysterectomy in infected patients to (1) labor and/or ruptured membranes of forty-eight hours or more associated with (a) temperature of 38°C (100.4°F) or more (b) chills, (c) positive blood culture and (d) bacteria in the amniotic fluid in large numbers, (2) repeated vaginal examinations with hands or unsterile gloves, (3) foul-smelling amniotic fluid, (4) labor after attempts at delivery, (5) when a bag, bougie or pack has been in the uterus, (6) more than twelve rectal or six vaginal examinations

cases. In safety it stands between the extraperitoneal and classic operations.

**Classic Operation.**—This is the easiest and simplest of the cesarean operations but has a much higher risk of peritonitis than the preceding ones. It may be performed at any time during pregnancy and is a quick operation. Classic section is useful in placenta praevia since the baby may be delivered without disturbing the placenta and causing further hemorrhage. The ease of technique makes it the most common of the cesarean operations used today, since surgeons who have had only scant training in obstetrics may perform the operation without difficulty. Unfortunately, the greater incidence of peritonitis produces poor results, when compared with the low segment operations, and its indications should be limited to premature delivery, hemorrhage and certain cases in which speed is essential, such as heart disease and impending fetal death due to pressure on the umbilical cord. It is contraindicated if there is any danger of infection, in the presence of labor and after membranes have ruptured, and it is more hazardous than a low segment operation even in an elective cesarean at term.

**Cesarean Hysterectomy.**—This operation should be limited to those cases in which uterine disease is present, such as placenta abruptio with couvelaire uterus, placenta accreta, severe postpartum hemorrhage, ruptured uterus and uterine tumors. I do not consider it to be indicated in infected labors since the maternal mortality in cases treated by this manner usually runs from 2 to 25 per cent. It may be elected occasionally as a method of terminating pregnancy and sterilizing simultaneously in medical conditions, such as hypertensive disease and pregnancy in women near 40 years of age or older.

**Vaginal Cesarean Section.**—With the development of other techniques there is a little need for this operation and the extensive incisions of the cervix through the internal os are as damaging as an abdominal incision, if not more so. Dührssen's incisions of the cervix, during delivery, are not to be classed as vaginal cesarean section.

#### SUMMARY

1. In considering indications for cesarean section an attempt has been made to use mathematical standards wherever possible.

2. With advancing knowledge there are fewer indications for cesarean section in general medical diseases and broader indications in local pelvic and obstetrical diseases.

3. The dangers of indiscriminate surgery are discussed and emphasis is placed on the fact that there is no substitute for thorough study, careful observation and skill.

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# SURGICAL COMPLICATIONS OF PREGNANCY

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THE pregnant woman is subject to any general surgical lesion as well as to the abnormalities peculiar to gestation which demand surgical therapy. While it has been established in recent years that surgical procedures may have but little effect upon pregnancy itself, there are special precautions in the preoperative management, surgical technic and after-care which are necessary.

The following is a brief outline of the various categories of surgical complications of pregnancy:

## I. Surgical Complications Due to Pregnancy Itself

- A. Ectopic gestation
- B. Rupture of uterus
- C. Placenta praevia
- D. Abruptio placenta
- E. Other indications for cesarean section wholly upon an obstetrical basis

## II. Surgical Complications Incidental to Pregnancy

- A. Lesions intrinsic to the genital tract
  - 1. Uterus
    - a. Myoma
    - b. Carcinoma
  - 2. Ovaries
    - a. Cysts
    - b. Solid tumors
    - c. Endometriosis
  - 3. Fallopian tubes
    - a. Infection
    - b. Tumors
  - 4. Lower genital tract
    - a. Lesions of vagina
    - b. Lesions of vulva
- B. Lesions extrinsic to the genital tract
  - 1. Head and neck
    - a. Intracranial lesions
    - b. Teeth and tonsils
    - c. Hyperthyroidism

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## 2. Thorax

- a. Bronchiogenic carcinoma
- b. Intrathoracic infections
- c. Cardiac surgery

## 3. Abdomen

## a. Appendicitis

- (1) Related conditions such as Meckel's diverticulitis, mucocele and regional ileitis

## b. Cholecystitis

## c. Intestinal obstruction

- (1) Carcinoma of gastrointestinal tract

## d. Hernia

## e. Kidney disease

## 4. Other regions

## a. Extremities

## b. Varicosities (extremities, anus, vulva)

The first group of surgical complications due to some abnormality of pregnancy itself is frequently discussed separately. This presentation takes up the other categories in which pregnancy complicates the picture of surgical conditions which may be encountered in nonpregnant women as well.

### LESIONS INTRINSIC TO THE GENITAL TRACT

**Uterus.**—*Myomas* occur in at least 20 per cent of women who have reached the age of 35 years.<sup>1</sup> Because of the frequency of this type of tumor in women of childbearing age it is commonly seen associated with pregnancy. Many myomas are small and cause no difficulty. However, in their presence the following complications may occur.

1. The chances of sterility are enhanced.
2. The incidence of abortion and premature labor are increased.
3. Rapid growth during pregnancy may take place giving rise to pressure symptoms.
4. Blockage of the pelvis giving rise to dystocia may occur.
5. Abnormal presentations of the fetus are more common.
6. Normal uterine contractions may be interfered with.
7. Postpartum hemorrhage is more frequent.
8. Delayed placental separation is more common.
9. The tumors may undergo degenerative changes during pregnancy or in the immediate puerperium.
10. Pedunculated tumors may undergo torsion and become gangrenous.

In spite of the possibility of serious complications, most pregnancies associated with fibroids are delivered normally. During the prenatal

course the most likely surgical emergencies are excessive size and degeneration of the tumors and torsion of the pedunculated myoma. The latter occurs in the subserous type of growth giving rise to sudden severe pain and sometimes shock. Immediate operation is necessary because gangrene and infection soon occurs. In these cases simple myomectomy is the procedure of choice and the pregnancy is usually not disturbed. There is no indication, however, for the removal during pregnancy of pedunculated fibroids which are without symptoms. Degeneration of large, rapidly growing fibroids is not an unusual complication. Pain and tenderness over the tumor involved are the usual signs and as the process advances a low grade fever develops as a result of necrosis of the growth. Treatment poses a different problem in these cases inasmuch as the surgical removal frequently calls for sacrifice of the uterus. Myomectomy in such patients is associated with great hemorrhage and hysterectomy is necessary in the far advanced cases. Conservative therapy with rest and sedation frequently tides the patient over until the baby is viable and not infrequently symptoms disappear entirely. In multiparas close to term with severe symptoms cesarean hysterectomy is the most efficacious procedure. In primiparas cesarean section may be done and the uterus allowed to remain until several months later when myomectomy may be performed. Myomectomy of a deep-seated tumor at the time of cesarean section is a dangerous procedure because of hemorrhage and rarely should be done. In early pregnancy myomectomy is a great deal safer and, even though abortion occurs, subsequent pregnancies may proceed to term. When abortion does not occur in such early cases following myomectomy, elective cesarean section close to term should be done to prevent the possibility of rupture of the uterus through the recent scars made in the myometrium.

Occasionally labor is obstructed by low lying myoma blocking the pelvic passageway. This usually arises from the cervix and cesarean section is mandatory. If the tumor happens to be pedunculated it may be removed at the time, otherwise a hysterectomy is done immediately after emptying the uterus or several months later, depending upon the condition of the patient and technical difficulty met with at the moment.

Even though delivery has been consummated normally there is still danger in the immediate postpartum period. Retained placenta is not infrequent, and postpartum hemorrhage, due to the poor contraction of the tumorous fundus, is much more common. A more delayed complication is that of degeneration of fibroids which is brought about by the severe ischemia which such tumors are subjected to by the forcible contraction of the myometrium about them. Because of this oxytocics are not without danger in the early puerperium although they can hardly

be withheld when there is excessive bleeding from a poorly contracting myomatous fundus. While most such cases will subside under a conservative regimen, the necrosis may be extreme and marked tenderness, leukocytosis and high fever develop. Hysterectomy should be done in such cases.

*Carcinoma of the Uterus.*—Squamous cell carcinoma of the cervix is the malignant lesion most frequently met with during pregnancy but even so it is quite rare. There are a few cases of adenocarcinoma of the cervix reported in the literature, and I have had experience with one such patient. Schumann<sup>2</sup> reported adenocarcinoma of the endometrium in a pregnant woman. Complication of carcinoma of the cervix with pregnancy is a doubly difficult one since both the malignancy and pregnancy should be treated in a way which will give the best chance of cure for the mother and at the same time afford the fetus a chance for survival if possible. The opportunity for carrying out such a program is not always feasible and depends upon the extent of the malignancy and the stage of the pregnancy. In far-advanced cases one may temporize for the sake of the child until viability has been reached inasmuch as the mother is already doomed. In earlier cases, however, therapy depends upon when in pregnancy the lesion is discovered.

When uncovered during the first trimester, therapy should be instituted immediately. An excellent method is that of subjecting the patient first to an adequate dosage of high voltage x-ray. This has the combined advantage of causing spontaneous abortion within a few weeks, sealing off the lymphatics thereby arresting the spread of the cancer and sterilizing any infection which might be present. This is then followed by the application of radium in adequate dosage. In my case of early adenocarcinoma of the cervix, I applied radium first, the capsule being easily inserted without dilatation or other manipulation of the cervix. Abortion occurred three weeks later and x-ray therapy was subsequently given. There has been no sign of recurrence in three years and ten months since this procedure was carried out although there is a moderate rectal stricture due to the irradiation. At the present time it is my opinion that patients with early carcinoma (stage I or early stage II), who are thin, in a young age group, and in good physical condition should be treated by radical surgical dissection and hysterectomy such as described by Meigs.<sup>3</sup>

Therapy in the second trimester of pregnancy is more difficult. Irradiation is less apt to bring about the abortion desired and if allowed to develop the fetus may be abnormal due to the effect of the rays upon the nervous system. Here hysterotomy may be done, and the lesion subsequently bombarded with large amounts of irradiation.

In the third trimester one may wait until viability whereupon the uterus should be emptied by cesarean section and the cervix treated immediately with x-ray followed by radium therapy. Vaginal delivery through a carcinomatous cervix is hazardous because of the possibility of furious hemorrhage due to tearing of the friable neoplastic tissue. Another danger is that infection, which is usually present in cervical carcinoma, may spread causing puerperal sepsis. Although it is commonly believed that malignant growths progress more rapidly when accompanied by pregnancy, this concept in reality has not been proved so that one may feel fairly confident that the results from therapy of this dread lesion during pregnancy should give us good results as in the nonpregnant woman. The most important consideration is early diagnosis. Every pregnant woman's cervix should be visualized at the first prenatal visit and repeatedly at intervals throughout pregnancy. Vaginal smears and biopsy of all suggestive lesions are obligatory, for without these aids diagnosis of early lesions is not possible and the best results cannot be attained.

**Ovaries.**—The presence of an ovarian tumor during pregnancy demands surgical therapy much more often than does myoma. The most likely complications from ovarian tumors in pregnant women are torsion, necrosis, rupture of the tumor causing peritonitis, hemorrhage, suppuration, excessive pressure and blocking of the presenting part during labor.

Any type of ovarian tumor may be present during pregnancy. *Simple retention cysts* are usually small and rarely cause difficulty, but *neoplastic cysts* are more dangerous and in fact may be malignant. *Dermoid cysts* are particularly treacherous inasmuch as they may erode into the bowel or may rupture causing a fatal peritonitis. When an ovarian growth the size of a grapefruit or larger is recognized it is usually safer to remove it surgically. If there is no torsion or other emergency it is better to wait until the fourth month since abortion is not unusual following ovariectomy during the first trimester. Whenever an ovarian tumor is removed the uterus should not be manipulated any more than is necessary.

Aside from acute torsion the most serious complications of ovarian tumors appear during labor. At this time the tumor may undergo pressure necrosis or rupture. When the growth impinges upon the pelvic cavity dystocia occurs and abnormal presentations are common. In such cases removal of the tumor by laparotomy is much safer than draining the cystic mass from below through the vagina inasmuch as there is no safeguard against spillage of its contents into the peritoneal cavity. When such a mass is removed during labor cesarean section is usually done. Not infrequently the long pedicled tumor will rise above the presenting part as labor ensues. Although vaginal delivery may then be accomplished without difficulty the tumor is apt to undergo torsion during the



immediate puerperium or may have been bruised to such an extent that necrosis, hemorrhage or suppuration occur and it is commonly necessary to remove the tumor during the postpartum period.

*Endometriosis* seldom accompanies pregnancy because it is so commonly associated with sterility. Surgical interference is rarely necessary when it is present although there may be abdominal pain and tenderness due to adhesions.

**Fallopian Tubes.**—*Salpingitis* is rarely associated with pregnancy since sterility is usually the rule although I have seen one case of bilateral tubo-ovarian abscess associated with large multiple myomas of the uterus and intrauterine pregnancy which was aborted at the fourth month. Pelvic adhesions due to chronic pelvic inflammatory disease may cause pain and discomfort. The treatment is conservative.

*Malignant growths* in the tube are extremely rare and should be surgically excised.

**Lower Genital Tract.**—The most common lesion of the lower genital tract which may have surgical significance is *Gartner's cyst of the vagina*. Gartner's cysts are thin-walled tumors which arise from the embryonic remains of Gartner's duct. They may become very large and in such instances cause dystocia. The most facile means of managing these tumors is to evacuate the contents with a syringe and dissect them out after delivery.

*Carcinoma of the vulva* is usually seen in postmenopausal women and is rarely encountered during pregnancy. When it is present a radical vulvectomy and gland dissection should be done and the pregnancy terminated by cesarean section close to term.

#### SURGICAL LESIONS EXTRINSIC TO THE GENITAL TRACT

**Head and Neck.**—Craniotomies for brain tumor or hematoma have been successfully performed upon pregnant women. The pregnancy should be disregarded when such procedures are indicated.

Mastoidectomy, tonsillectomy and tooth extractions have been performed during pregnancy without affecting the latter. It is especially important to extract abscessed teeth during pregnancy as soon as they are found so as to prevent foci of infection or subsequent large abscesses or osteomyelitis of the jaw.

*Hyperthyroidism*, while relatively uncommon during pregnancy, is a complication which warrants careful consideration. Until rather recently, therapeutic abortion was sometimes done in such cases in certain sections of this country. This practice has been, or at least should be, practically abandoned. During normal pregnancy the thyroid enlarges slightly and there is an increased basal metabolic rate to +20 or +30 per cent. Because

of this some authorities believe that thyrotoxicosis is made worse by pregnancy. On the other hand, it has been pointed out that the fetus feeds upon the mother's thyroid, and there are instances in which the hyperthyroidism has apparently been improved by pregnancy.

Lugol's solution in a dosage of 10 minims three times a day is greatly beneficial in nearly all cases and its use may make surgical delay quite safe until after delivery. However, if, after a trial with iodine the condition is becoming worse or if cardiac or other complications are present, thyroidectomy should be performed. This operation seldom affects the pregnancy if done after the first trimester. Mussey and Plummer<sup>4</sup> reported excellent results from the Mayn Clinic with such a regimen.

Recently the newer drug propylthiouracil has been used extensively in thyrotoxicosis. Little is yet known concerning its effect upon pregnancy. At the Jefferson Hospital, as this paper is submitted, we have a patient under treatment with this drug. She is a 36 year old Gravida IV Para III who had the typical symptoms of toxic hyperthyroidism when first seen early in pregnancy. The basal metabolic rate varied from +60 to +85 per cent. With thiouracil great clinical improvement has taken place and the most recent basal rate was +10 per cent. The dosage has been 300 mg. per day given in six divided doses of 50 mg. each.<sup>5</sup> While this mother has tolerated the drug well and has received a splendid result from its use, the outcome of the delivery with especial interest in the condition of the fetus is being awaited. It has been feared in some quarters that the use of this drug during pregnancy might cause cretinism of the offspring. Until more experience has been gained with this drug, iodine and surgery should remain as the therapeutic methods of choice in hyperthyroidism associated with pregnancy.

**Thorax.**—Inasmuch as thoracic surgery is a relatively new field, few cases have been reported done in association with pregnancy. Lobectomy<sup>1</sup> and pneumonectomy have been successfully performed during gestation and there is no reason to believe that pregnancy is affected adversely by such procedures. One might theorize that postoperative management following radical lung or cardiac surgery might be complicated by the encroachment upon the diaphragm of the uterus close to term.

**Abdomen.**—*Appendicitis* probably occurs as frequently during pregnancy as at other times although Baer, Reis and Arens<sup>6</sup> reported the incidence during pregnancy to be but 0.17 per cent in 16,543 deliveries at the Michael Reese Hospital, while over the same period of time the incidence was 1.6 per cent in nonpregnant individuals. There is little doubt but that suppurative appendicitis is a much more serious disease when it is associated with pregnancy. As pregnancy advances the mortality increases. De Lee had a mortality of 40 per cent from this com-

plication in late pregnancy and mentions the following points as factors involved in making the combination of pregnancy and appendicitis a serious one:<sup>7, 8</sup>

1. The fact that protective adhesions do not form so well because of dislocation of relation of appendix, the gut and omentum by the uterus
2. Inflammatory processes tend to be more acute because of increased general vascularity of the pelvic abdomen
3. Because of this factor, thrombosis and phlebitis tend to occur more frequently.
4. Because of the upward dislocation of the appendix, suppuration, when it occurs, involves the higher and less resistant portions of the peritoneum
5. Because the uterus occupies the greater part of the abdominal cavity, drainage of pus is less facile and it tends to burrow more extensively.
6. Because of distention of the abdomen by the uterus the occurrence of intestinal distention in connection with appendicitis or the operative treatment for it, causes more embarrassment of respiration and more frequent pulmonary complications
7. For the same reason intestinal obstructive symptoms are more frequent and occur earlier
8. There is considerable risk of bacterial infection of the placental site

It is therefore quite obvious that early operative interference is mandatory in order to obtain the best results. This depends upon early diagnosis which is not always easy in the nonpregnant individual and is more difficult during gestation. Symptoms are right-sided pain and tenderness, nausea and vomiting, low grade fever and leukocytosis. When it is considered how frequently there is transient abdominal pain during pregnancy, it is readily understood how appendiceal pain may easily be misinterpreted. If the physician always keeps in mind the possibility of appendicitis and the fact that pain and tenderness may be higher in the abdomen as pregnancy advances, often at or above the level of the umbilicus, not many cases will be missed. Rigidity is not as common a finding because of the physiologic distention of the abdominal wall. Nausea and vomiting are such common accompaniments of pregnancy that their presence does not lend as much weight in making a diagnosis as in the nonpregnant woman. Likewise the physiological leukocytosis of gestation discounts the value of the white blood count although a great increase in polymorphonuclears and a definite shift to the left are diagnostic aids.

Right-sided pyelitis and ureteritis is the condition most often confused

with appendicitis in the gravid woman. This condition may give right lower quadrant tenderness with dysuria or pyuria early in its development. However, it is more commonly associated with a shaking chill, higher fever and usually is accompanied by costovertebral angle tenderness and pus in the urine from which the diagnosis can be established. Appendicitis is especially difficult to diagnose in the early puerperium. At this time after-pains, parametritis and the residual tenderness usually following delivery may be responsible for fatal delay in diagnosing inflammation of the appendix.

Whenever appendicitis is suspected during pregnancy operation is indicated just as soon as other conditions can be reasonably ruled out. The pregnancy is seldom affected and it is much better to operate and be mistaken in the diagnosis than to procrastinate and take the chance of peritonitis developing. Early in pregnancy appendectomy is usually a simple matter, but as pregnancy progresses difficulties are more apt to arise. Late in gestation a higher incision than usual is very efficacious. If it is thought that drainage may be necessary a muscle-splitting incision of the McBurney type is best.

There has been a great deal of discussion as to whether appendectomy done near term or during labor should be accompanied by cesarean section. Unless there is disproportion or some other obstetrical indication present, the abdomen should be closed following the appendectomy and the patient allowed to deliver normally. It has repeatedly been shown that a carefully closed incision suffers no ill effects even though delivery takes place within a few days or even a few hours after the operation. Cesarean section in the presence of generalized peritonitis is a particularly pernicious practice and a number of tragedies have occurred because the infection soon involved the entire uterus. Because of this there are those who still perform cesarean hysterectomy in face of this complication. It is my opinion that, when cesarean section is indicated in the presence of generalized peritonitis, extraperitoneal cesarean section should be performed first, followed by a high muscle-splitting incision with removal of the appendix and the institution of drainage. In this way the uterine incision and placental site are not exposed to infection and the uterus is preserved.

Occasionally the abdomen is opened and a normal appendix is found. In such cases it is important to explore for another lesion. The most common intra-abdominal conditions which may be present are Meckel's diverticulitis, cholecystitis, ruptured peptic ulcer, intestinal obstruction, regional ileitis and mucocele of the appendix. Appropriate operative interference is indicated in the treatment of ruptured ulcer, obstruction and diverticulitis, while the other lesions may often be treated conservatively.

I am acquainted with a case diagnosed as appendicitis during the latter months of pregnancy, where the abdomen was closed after a normal appendix was visualized. The patient subsequently died of generalized peritonitis and at autopsy a ruptured Meckel's diverticulum was found. Mucocoele of the appendix is uncommon but when it is large and inflamed causing brawny induration of the surrounding bowel there is danger of its rupture with resulting generalized pseudomyxoma peritonei. Such a lesion cannot be removed safely. I recently performed a transverse ileocolostomy in such a case so as to short-circuit the fecal stream and allow the lesion to subside. The appendix was removed several months later and had shrunk to almost normal size.

*Gallbladder disease* is two or three times as common in women as it is in men. It is known that 90 per cent of women operated upon for gallstones have borne children,<sup>9</sup> and it is thought by many that pregnancy is a factor in their development. Even so, cholecystitis occurs infrequently during pregnancy and usually may be treated conservatively. The main indications for surgical interference are empyema of the gallbladder and chronic calculous cholecystitis with common duct obstruction and jaundice. The pregnancy is seldom disturbed.

*Intestinal obstruction* is a serious complication of pregnancy and presents difficulties in diagnosis. Immediate surgery is indicated although this is often delayed overlong. Volvulus, intussusception, strangulated hernia, carcinoma and adhesions from previous surgery or infection are the common causes of obstruction. Intestinal adhesions to the uterus may be the cause of increasing obstruction as the uterus enlarges, putting more and more tension on the gut. In late pregnancy the large uterus may make operation difficult. This is especially true of carcinoma of the rectum or lower sigmoid. When such a lesion is present the uterus should be emptied at once so that radical surgery may be applied to the lesion as soon as possible. It frequently is most efficacious to terminate the pregnancy by cesarean section and at the same time gain further knowledge concerning the lesion by visualization and palpation.

The various types of *hernia* frequently are associated with pregnancy. They are often made larger by the relaxation typical of this condition but seldom become incarcerated<sup>9</sup> because the uterus draws the abdominal contents upward as it enlarges and covers the hernial opening adequately during labor. When adhesions to the sac are present, great pain and even obstruction may be caused by the traction exerted. In the event of incarceration surgical treatment is instituted just as in nonpregnant individuals.

*Nephrectomy* may be done during pregnancy without affecting preg-

nancy any more frequently than does the performance of other major operations upon other unrelated organs.

*Amputation of an extremity* is not more dangerous during pregnancy than at other times. Such an operation occasionally must be done because of severe trauma or malignancy.

*Varicose veins* are common during pregnancy but are pronounced in only about 20 per cent of pregnant women.<sup>9</sup> The most common sites are the lower extremities, vulva and about the anus where the hemorrhoidal vessels are frequently involved. These give rise to symptoms of fullness, heaviness and pain. The complication to be most feared is hemorrhage due to rupture of one of the vessels. Pressure, elevation, ice bags and suture may be used to control this. Thrombosis, infection and ulceration may also occur. The treatment of all these conditions is predominantly conservative. Surgical procedures are rarely needed and are usually limited to venous ligations and the enucleation of thrombosed external hemorrhoids. It must be remembered that most varicosities disappear after delivery and even the worst are greatly improved.

#### GENERAL CARE OF PREGNANT PATIENTS WITH SURGICAL COMPLICATIONS

The performance of major surgical operations during pregnancy has been made comparatively safe in recent years by advancements in surgical technique, anesthesia and preoperative and postoperative care. Unlimited blood transfusions, chemotherapy, antibiotics, dependable hormones and a more astute understanding of body chemistry, nutrition and fluid balance have added immeasurably to the safety of these procedures. The use of local anesthesia whenever possible and the comparative safety of continuous spinal anesthesia have also been of great value. The newer modifications of extraperitoneal cesarean section techniques have made suprapubic delivery in the face of generalized peritonitis safer and more easily possible without sacrificing the uterus.

After any major operation upon a pregnant woman, moderate sedation should be maintained for several days. Progesterone, 10 mg. by hypodermic, should be given daily. If the operation is performed during the first trimester the dose should be doubled. Pregneninolone may be given by mouth but the dosage should be six times as great as that of progesterone. Some add 10,000 to 25,000 units of estradiol to the progesterone each day. Others use huge doses of stilbestrol alone. Early ambulation is contraindicated in this group of patients unless there is some constitutional reason for invoking it. When all of these safeguards are used the fetal salvage and the safety for the mother are enhanced.

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# **SYMPOSIUM ON STREPTOMYCIN IN THE SURGERY OF TUBERCULOSIS**

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## **THE USE OF STREPTOMYCIN IN RESECTION FOR PULMONARY TUBERCULOSIS\***

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### **INTRODUCTION**

EXTIRPATIVE surgery has as its objective the complete removal of a pathologic process. This ideal must be compromised in many instances depending on the tissue involved, the nature of the process concerned, the phase of therapeutic evolution, and such imponderables as the immunobiologic balance.

Pulmonary parenchyma is becoming increasingly accessible to extirpative therapy. It has been hoped that excision might approach the ideal in the treatment of pulmonary tuberculosis. Thoracoplasty is certainly a compromise measure. The therapeutic value of surgical collapse is established, but its logic is the antithesis of ideal. Normal tissue is sacrificed, and the pathologic tissue remains. Bed rest, the bulwark of tuberculosis therapy, is interrupted by multiple, major surgical procedures. Resection is performed in one operation with removal of the major pathologic focus. The surgical recovery is usually rapid and uneventful.

With increasing experience it is becoming possible to evaluate extirpative measures in the treatment of pulmonary tuberculosis.<sup>3, 12, 13, 14, 15</sup>

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\* Submitted for publication January 1, 1948. Since that time six additional months observation is available. Only one patient of the cases reported here is now hospitalized (Case VIII, R. F., No. 20,087). The surgical experience with streptomycin in this institution is now approaching two years' duration and includes the treatment of more than 300 patients. Four additional resections have been performed without any complication—three lobectomies and one segmental resection (apical and posterior subapical segments).

Since the manuscript was prepared there have been other publications regarding the use of streptomycin in pulmonary resection for tuberculosis. Some of the opinions expressed here have been mentioned. Reference has been made to the possibility of segmental resection. Such independent expression seems to lend some credence to the impressions gained here.



Some surgical indications are established, and others are presumptive. Much of the experience recorded thus far has been discouraging. These reports show that resection frequently fails to cure. The late death rate is high, and tuberculosis recurs in a large percentage of the survivors. It still seems logical that in any one given patient with a lesion which may be collapsed or excised, greater benefit *should* result if the diseased tissue is removed. Complete extirpation of the tuberculous process is usually impossible, and surgical success is attained only when the patient can cure his residual disease. This is a function of the immunobiologic balance. Unless it is weighted in favor of the patient, the extirpative measures will not cure. Technical refinements, antibiotic and chemotherapeutic agents have been added recently to support excision therapy. Sufficient time has not passed to evaluate fully their effect.

The antibiotic, streptomycin, was isolated by Schatz, Bugie and Waksman<sup>1</sup> in 1943, and subsequently shown to inhibit most strains of *Mycobacterium tuberculosis*.<sup>2</sup> Clinical trial of this agent in the medical management of tuberculosis supported the experimental findings.<sup>3</sup> In most cases, the tuberculous process was suppressed but not cured. Favour<sup>4</sup> and his associates assume from work with laboratory animals that the antibiotic is effective only against extracellular organisms. This is consistent with the good clinical results of streptomycin in exudative disease, fresh milary, and hyperemic nonfibrous lesions, and explains the poor clinical results in fibrous and caseous lesions.

Early clinical experience suggested that streptomycin might be a valuable adjunct to the surgical treatment of pulmonary tuberculosis.<sup>5, 6</sup> Theoretically, streptomycin would favorably weight the important immunobiologic balance (a) by inhibiting the development of new intrapulmonary or extrapulmonary disease from contamination or extension incident to the surgical maneuvers, and by (b) suppressing the reactivation of quiescent diseased foci manipulated during surgery or subjected to stress during readjustment of the thorax. Early clinical support of this theoretical protective action of streptomycin was afforded by the report of Glaver and his associates.<sup>7</sup> Experience with the use of streptomycin in this hospital is also encouraging.

The patients who were given streptomycin because their treatment required extirpative surgery are reported here. Nine resections for pulmonary tuberculosis performed during the past year consist of three pneumonectomies and six lobectomies. One additional pneumonectomy was performed in a patient presenting the differential diagnosis of cancer and tuberculosis. The series is numerically insignificant, and the period of observation is incomplete, however, the cases are clinically interesting and certain observations may be of value in excision therapy.

## THE INDICATIONS FOR RESECTION

The indications for resection in this clinic have been tuberculoma, symptomatic tuberculous bronchiectasis, collapse failure, bronchial stenosis, secondary suppuration, giant cavitation, and suspicion of neoplasm. Frequently, among the resection cases, more than one of the above factors was present in the same patient. Table 1 lists the indications used and shows their multiplicity in several patients. Other indications for resection are recognized but have not been utilized during our streptomycin experience.

Lobectomy was always performed in preference to pneumonectomy in accordance with the philosophy that the *entire* tuberculous process could seldom be extirpated. Additional segments or lobes were removed only

TABLE 1  
MULTIPLICITY OF INDICATIONS FOR RESECTION IN TEN PATIENTS

Case No . . . . .	Lobectomy						Pneumonectomy			
	2	4	6	7	8	9	1	3	5	10
Tuberculoma . . . . .	x						x			
Tuberculous bronchiectasis . . . . .		x					x			
Collapse failure . . . . .			x	x		x		x	x	
Bronchial stenosis . . . . .						x				
Secondary suppuration . . . . .			x		x					
Giant cavitation . . . . .					x		x			x
Suspicion of neoplasm . . . . .										x

when definite independent indications existed or when pneumonectomy was necessary for the removal of the paramount pathologic focus. This concept occasionally necessitated dissecting in segmental fashion, and interlobar fissures were sometimes developed through grossly diseased, even caseous tissue.

## OPERATIVE REGIMEN

The operative regimen is outlined to enable correlation of the conditions of resection with those of other groups.

Streptomycin is begun one week before operation. The dose has varied with different protocols of the Veterans Administration Committee on Streptomycin. Eight patients received 1.8 to 2 gm. intramuscularly each day as multiple injections every four hours. One patient received 1 gm. intramuscularly each day in divided doses every twelve hours. One patient received only intrapleural streptomycin. Acrosol penicillin, 60,000 units, is given every four hours preoperatively for one week, and during

the last three days it is supplemented by intramuscular penicillin in the same dose. Transfusions are given as indicated to combat anemia. Posteroanterior and lateral roentgenograms of the chest are obtained the day before operation.

Immediately before the operation the patient is bronchoscoped, and secretions are aspirated from the tracheobronchial tree. Closed intratracheal anesthesia is used with cyclopropane induction, maintained with oxygen and ether. Tracheobronchial secretions are aspirated by the anesthetist frequently during the operation. The posterolateral rib resection thoracotomy is employed. Adjacent intercostal bundles are blocked with 2.5 cc. of nupercaine in oil. The intercostal nerve of the resected rib is divided or traced to the dorsal root ganglion which is excised. The individual vessels of the hilum are ligated with silk. The bronchus is closed with multiple end-on silk sutures. A flap graft of parietal pleura is developed to cover the bronchial stump and, following lobectomy, the bronchial stump is further buttressed with immediately adjacent pulmonary parenchyma. A fenestrated intercostal tube is introduced in the midaxillary line and sutured high in the pleural cavity after lobectomy. The chest wall is closed in layers with interrupted chromic No. 0 catgut and black silk sutures. One gram of streptomycin and 100,000 units of penicillin are instilled into the intrapleural space. During the operation 1500 to 2000 cc. of compatible whole blood is given. Immediately postoperatively a bronchoscope is passed. The secretions are aspirated, and the bronchial stump is examined.

After operation oxygen is administered as necessary, but overuse is avoided as it thickens secretions and suppresses cough and respiration. Pharyngeal and tracheal aspirations effectively stimulate deep breathing and coughing. The intercostal tube is removed within forty-eight hours after operation.

Following pneumonectomy the chest is closed without drainage. The intrapleural space is kept dry and the pressures balanced by frequent thoracenteses. The ipsilateral phrenic nerve is interrupted when pneumonectomy is performed.

If pleural contamination is suspected, 1 gm. of streptomycin is instilled into the pleural cavity three times per week for two weeks.

Overdistention of the other lobes after lobectomy is rigidly avoided by maintaining a limited anterior apical intrapleural pneumothorax until an appropriate thoracoplasty can be performed. Strict bed rest is maintained for a minimum of three months.

## RESULTS

Eight of nine patients subjected to resection for pulmonary tuberculosis are clinically well and have negative sputum. None shows any evi-

dence of active tuberculosis. No one has tuberculous spread, empyema, fistula or wound infection.\* Four of these patients have been discharged from the hospital as arrested or apparently arrested cases by the standards of the National Tuberculosis Association. Four patients are still hospitalized, but they are clinically well. One fatality occurred in a desperately ill patient for whom all observers considered the nonsurgical prognosis hopeless. The patient had received streptomycin for more than 170 days on the medical service because the radiographic picture suggested miliary tuberculosis. Streptomycin was reinstituted prior to surgery as in other cases, but it was felt that no therapeutic benefit could be expected after such prolonged previous administration. Lobectomy was well tolerated by the patient, but excision failed to abate his downhill course and he died thirty-five days after operation.

Two of the ten patients in this series had ipsilateral postoperative atelectasis. One patient showed good aeration of the affected lobes after intratracheal catheterization. The other patient developed a patchy pneumonitis in the lower lobe of the left lung. His postoperative course was characterized by fever and tachycardia for five days. These patients have been followed twelve and four months respectively. Neither has clinical or radiographic evidence of tuberculous spread to the affected zones.

The patient who was operated upon for suspicion of neoplasm was referred to this hospital for pulmonary tuberculosis. Medical observation extended over a period of fifteen months. He was reported to have had a positive sputum in a previous hospital and had received temporary collapse measures for tuberculosis. At operation a bronchogenic carcinoma of the left upper lobe bronchus was found with a distal giant cavity. A left pneumonectomy and hilar resection were performed. While it is possible that active pulmonary tuberculosis and carcinoma coexisted, it was felt that this patient's disease was primarily neoplastic. Streptomycin was discontinued postoperatively and the patient was discharged after the surgical recovery.

### CASE SUMMARIES

Group statistics are the reflection of multiple individual cases. In tuberculosis the individual variants are great. The progression of a radiographic lesion, the individual host response, and the results of therapy are difficult to prognosticate and standardize. This protean nature renders tuberculosis unsatisfactory for mass statistical data and tedious for complete individual case review. Extirpative surgery in pulmonary tuberculosis requires further observation and case segregation for sig-

\* Except as corrected by the footnote appended to Case VIII, R. F., No. 20,087.

nificant group statistics, therefore, the operative rationale and result in the individual case must be considered. A statement of rationale is included with each case summary and may give the reader more insight into the status of extirpative therapy than general discussion.

**CASE I (A M, No 19,142)**—The patient is a 21 year old white, single male. After the onset of chest pain aboard ship in April 1945, he was transferred to a Naval Hospital. Chest roentgenogram revealed a left apical cavity and patchy infiltration of the left upper and right lower lobes. A review of his 1943 photo-fluorographic films showed an infiltrate in the left lower lobe. The induction of left artificial pneumothorax was unsuccessful, and left phrenicostoma was performed after four months of bed rest without improvement.

The patient was admitted to this hospital in May 1946. His general condition

atelectasis of the left lower lobe. On the right there was fibrogranular infiltration from the second rib upward.

Bronchograms revealed advanced left lower lobe bronchiectasis and showed normal bronchi on the right. In an oblique film at this time an additional large cavity with a fluid level was observed in the left lower lobe.

Left pneumonectomy was performed in October 1946. At operation no free pleural space was found. It was necessary to force a cleavage plane along the posterior gutter, and in so doing a large cavity was entered. The cavity wall actually infiltrated the intercostal spaces so that removal without rupture was impossible. The cavity wall was cauterized with 95 per cent phenol, cleaned with alcohol, and irrigated thoroughly. The chest wall was closed without drainage. One gram of streptomycin and 100,000 units of penicillin were instilled into the intrapleural space.

Following left pneumonectomy, thoracentesis was performed three times a week for four weeks. Fluid was withdrawn, and antibiotics were injected. Only 0.5 gm. of streptomycin was available during the first two weeks. Later 1 gm. was used after each thoracentesis. A smear of the chest fluid was positive for acid-fast bacilli. After six weeks no fluid was obtained.

After three months of bed rest, graduated exercises were started. Left thoracoplasty was performed in May 1947 with removal of posterolateral segments of ribs two to five. The patient was discharged as an arrested case July 1947. He is attending drafting school, feels well, and his tuberculosis is arrested.

**Operative Rationale**—Multiple giant cavities, tuberculomas and tuberculous bronchiectasis were the indications for resection. Pneumothorax had failed. Surgical collapse offered nothing for the bronchiectasis or for the tuberculomas, and giant lower lobe cavities are difficult to collapse by thoracoplasty. After the demonstration of normal bronchi on

the right, these multiple factors made pneumonectomy the rational therapeutic approach.

**CASE II (C. C., No. 19,565).**—The patient is a 39 year old white married male. Chest disability began in 1939 with pain. Prior to admission, he was followed in Army Hospitals with periodic roentgenograms and sputum examination. He had one positive sputum as an outpatient.

The patient was admitted to this hospital in August 1946. Examination showed him to be in good general condition. There were no significant physical abnormalities. Chest roentgenogram showed numerous discrete, fibronodose and calcific bodies in the right upper lobe. The largest of these measured 2.5 cm. There were bilateral perihilar calcifications. The patient was discharged after observation with a diagnosis of minimal inactive pulmonary tuberculosis. Guinea pig inoculations made during the hospital stay were positive for tuberculosis, and he was readmitted.

In January 1947, a right upper lobectomy was performed. Streptomycin, 18 gm. per day, was given one week before and two weeks after operation. On the first postoperative day the patient had right middle and lower lobe atelectasis. This cleared after intratracheal aspiration, and his recovery was without further complication. Right thoracoplasty was done one month later with removal of ribs two to five. Prescribed bed rest and graduated exercises were completed, and the patient was discharged from the hospital as an arrested case. He has had no recurrence of active pulmonary tuberculosis. (Figs. 410, 420 and 421.)

*Operative Rationale.*—Resection is often the treatment of choice for a tuberculoma. Multiple tuberculomata in one lobe, giving intermittent positive sputum, made lobectomy rational treatment.

**CASE III (E. L., No. 18,725).**—The patient is a 27 year old white single male. The symptomatic onset of his disability was in March 1945 with cough. He was treated in an Army Hospital with bed rest until transferred to this institution in October 1945.

Physical examination on admission showed the patient to be in good general condition, with abnormalities limited to the chest. The roentgenogram showed giant cavities in the left upper lobe, and a probable cavity in the apex of the left lower lobe. Sputum was positive for tubercle bacilli on direct smear. The serial chest films showed increasing excavation.

Bronchoscopy was performed, and tuberculous endobronchial disease was found in the left main bronchus.

Left thoracoplasty was begun in April 1946. After resection of seven ribs in three stages, a large cavity was still open below the collapsed area. An additional stage of thoracoplasty removed the eighth and ninth ribs. This was supplemented with a left phrenic paralysis and pneumoperitoneum which was discontinued after six months trial as ineffective.

Fig 419

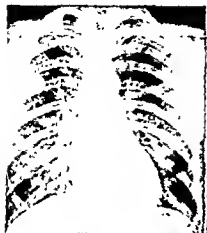


Fig 420



Fig 421

Fig. 419 (Case II) —A preoperative chest roentgenogram showing tuberculomas in the upper lobe of the right lung

Fig 420 (Case II) —A chest roentgenogram showing selective thoracoplasty collapse after resection

Fig 421 (Case II) —A photograph of the upper lobe of the right lung showing the tuberculomas

Left pneumonectomy was performed in February 1947. Streptomycin, 2 gm. per day, was given one week before and two weeks after operation. The patient's

Fig. 422



Fig. 423



Fig. 424

Fig. 422 (Case III).—A preoperative chest roentgenogram showing multiple large cavities in the left lung field.

Fig. 423 (Case III).—A chest roentgenogram after collapse failure showing a left nine-rib thoracoplasty, left phrenic paralysis, and pneumoperitoneum.

Fig. 424 (Case III).—A photograph of the resected left lung with multiple cavities, tuberculomas, and tuberculous bronchiectasis.

recovery was without complication. He completed the prescribed bed rest and graduated exercises and was discharged as an arrested case. He has had no recurrence of active pulmonary tuberculosis. (Figs. 422, 423 and 424)



*Operative Rationale*—Thoracoplasty, phrenic paralysis, and pneumoperitoneum failed to close a lower lobe cavity. The entire left lung was collapsed and nonfunctional, but it was still the pathological focus giving rise to positive sputum. The contralateral lung had no active disease. Resection seemed mandatory.

CASE IV (H. B., No. 19,359)—The patient is a 21 year old single male. His disease began with cough and chest pain in August 1945 and he was hospitalized with a diagnosis of atypical pneumonia. Six weeks later he had hemoptysis and was found to have soft infiltration of the lower two-thirds of the right lung. His sputum was positive for tubercle bacilli. A subsequent spontaneous pneumothorax collapsed the right lung. A bronchopleural fistula developed with a tension pneumothorax and mixed empyema. Needle aspirations were performed and the right upper lobe reexpanded. He continued to be febrile, developed a draining sinus of the right chest wall, a chronic sore throat, and hoarseness.

The patient was transferred to this hospital in August 1946. He appeared acutely and chronically ill. His temperature was 101° F. There was a right hydro-pneumothorax with two draining sinuses. Sputum was raised in copious amount and was positive for tubercle bacilli on direct smear. Chest roentgenograms revealed a diffuse granular stippling throughout the entire left lung and the right upper lobe. The lower half of the right lung was densely opaque, and the visceral and parietal pleurae were covered with a shaggy exudate. Fluid covered the dome of the diaphragm. The trachea deviated to the right.

The presence of a patent bronchopleural fistula and mixed empyema was verified, and the right eighth rib was resected for dependent open drainage of the empyema. The right lower lobe was shrunken and nodular with apparent multiple abscesses.

Bronchoscopy showed marked tuberculous endobronchial disease with ulceration and stenosis of the right lower lobe bronchus.

Streptomycin was given because military tuberculosis was suspected. He received 1.8 gm. per day for 147 days, and 2 gm. per day for another twenty-five days. Penicillin and sulfadiazine were given concomitantly. Frequent bronchoscopy was performed, secretions were aspirated and the right lower lobe bronchus lavaged with penicillin. These procedures were of minor benefit. The patient had daily fever of 101° to 105° F., was losing weight, and failing rapidly.

In May 1947, right middle and right lower lobe lobectomy was performed through the previously resected eighth rib bed. There was a thick, necrotic cortex lining the empyema space. Undrained loculations were not found. The hilar structures were isolated with difficulty. The bronchial stump was covered with an oxidized cellulose pack. The chest wall was closed in the usual manner with intercostal tube drainage, and antibiotics were injected. Toward the end of the operation the patient had moderate hypotension, but this responded to replacement therapy. Postoperatively right phrenic paralysis and pneumoperitoneum were instituted. Streptomycin, 2 gm. per day, was given for ten days during the surgical course. On the thirteenth postoperative day the bronchus reopened.

The empyema space was well drained and no new parenchymal shadows developed. The patient continued to run his usual febrile course with daily temperatures of 100 to 103 F. He was anorexic and dyspneic. He died on the thirty-fifth postoperative day.

*Operative Rationale.*—Resection may be curative for tuberculous bronchiectasis with distal suppuration. These indications existed in this patient, but they were complicated by bronchopleural fistula, undrained mixed empyema, possible miliary tuberculosis, and his desperately ill condition. The priority of all these factors could not be established early. The benefit of streptomycin was exhausted without improvement. Conservative measures failed. The pathological processes in the right middle and right lower lobes were thought to be the cause of both local and systemic disease. Excision of this focus seemed to offer the only hope for cure.

**CASE V (D. P., No 19,583)**—The patient is a 23 year old white married male. Pulmonary tuberculosis developed with the classical symptomatology in September 1945. A roentgenogram taken at this time showed soft infiltrations throughout the upper two-thirds of the left lung and the upper one-half of the right lung. Left artificial pneumothorax was induced, and subsequent roentgenograms showed apical cavitation with intrapleural adhesions. Closed pneumonolysis was performed in two stages and was followed by a pleural effusion of brief duration. By July 1946 the infiltrations had faded, no cavities were visible, and the patient's sputum was negative. He was discharged home.

The patient was admitted to this hospital six months later. He was in good general condition, and the only significant physical finding was the left pneumothorax. Sputum was positive for tubercle bacilli. The admission roentgenogram showed 60 per cent collapse of the left lung with honeycombing in the collapsed portion. The left diaphragm was elevated and fixed. Bronchoscopy showed moderate hyperemia of the left main stem bronchus. Pneumothorax refills were required only every four to six weeks. Within four months after admission there was definite cavitation in the hilar region of the left lung. Under positive pressure pneumothorax this cavity enlarged. Pneumothorax was discontinued, but the lung showed no tendency to expand.

A left pneumonectomy was performed July 1947. Streptomycin, 2 gm. per day, was given ten days before and twenty days after operation. Left thoracentesis was performed three times a week for two weeks with aspiration of the fluid and injection of antibiotics. Left thoracoplasty with resection of ribs two to eight and partial scapulectomy was performed in two stages two months later. The patient was discharged from the hospital as an apparently arrested case. His sputum is negative and the right lung shows no active disease.

*Operative Rationale.*—Resection was performed for collapse failure. A cavity developed and increased in size under positive pressure pneumo-

thorax. The lung would not reexpand. Even so, total thoracoplasty would not have improved the collapse. Resection seemed to be the only rational therapy.

**CASE VI (E. C., No. 19,089)**—The patient is a 29 year old white married male. A routine chest roentgenogram in August 1945 revealed pulmonary tuberculosis. There was patchy infiltration of the left upper lobe with a 2 cm cavity and fibrogranular infiltration of the right upper lobe. Left artificial pneumothorax was begun one month later and continued until he was admitted to this hospital April 1946.

Examination showed the patient to be in good general condition. Physical abnormalities were limited to the chest. Sputum was positive for acid-fast bacilli on direct smear. Chest roentgenograms showed a left pneumothorax with 50 per cent collapse and a moderate amount of fluid at the base. Intrapleural adhesions could be visualized, and the cavity in the left upper lobe was open.

A closed pneumonolysis was performed with partial success. The cavity changed shape but increased in size. Pneumothorax was discontinued, and the lung was reexpanded. Left thoracoplasty was performed in three stages, resecting ribs one to eight. Five months later the patient still had positive sputum and a slitlike cavity in the left apex. Bronchoscopy showed normal endobronchial mucosa. A two-stage revision thoracoplasty was done with increased apical collapse. Subsequent tomography showed no cavitation underlying the thoracoplasty. The patient's sputum continued to be positive. Bronchoscopy now revealed tuberculous endobronchial disease at the level of the left upper lobe bronchus. Streptomycin, 2 gm per day, was given. Frequent bronchoscopy showed progressive improvement of the endobronchial disease, however, he continued to have positive sputum.

After sixty days of antibiotic therapy a left upper lobe lobectomy was performed. Resection was accomplished without undue incident.

Postoperatively the patient developed a patchy pneumonitis of the left lower lobe with fever and tachycardia. No specific pyogenic organism could be cultured. After five days of fever ranging between 100° and 102°F, the temperature fell to normal by lysis. Streptomycin was discontinued two weeks after operation. The patient is now clinically well with negative sputum, and has no radiographic evidence of tuberculous spread nor active pulmonary tuberculosis (Figs 425, 426 and 427).

**Operative Rationale**—Failure of sputum conversion by collapse measures necessitated resection. Pneumothorax, pneumonolysis, thoracoplasty, revision thoracoplasty and streptomycin therapy failed. Tuberculous endobronchial disease and tuberculous bronchiectasis under the collapse caused persistent positive sputum. Extirpation seemed to be necessary for cure.

**CASE VII (H. S., No. 19,607)**—The patient is a 50 year old white married male. Pulmonary tuberculosis of the left upper lobe was discovered by routine

Fig. 425

Fig. 426



Fig. 427

Fig. 425 (Case VI) —A chest roentgenogram showing the failure to close cavities in the upper lobe of the left lung by pneumothorax.

Fig. 426 (Case VI).—A chest roentgenogram after collapse failure from a seven-rib left thoracoplasty.

Fig. 427 (Case VI) —A photograph of the resected upper lobe of the left lung showing tuberculous bronchiectasis and tuberculomas.

roentgenogram in 1944. The patient was followed for one year without evidence of activity. A pulmonary hemorrhage occurred in April 1945; a left upper lobe cavity was discovered, and the patient had positive sputum. Artificial pneumo-

thorax was unsuccessful. In September 1945 a left thoracoplasty was performed in two stages with resection of seven ribs. Nine months after operation, the patient returned to the hospital with a draining sinus in the operative incision. The sinus healed spontaneously, but five months later a fluctuant mass developed under the thoracoplasty incision, and the sinuses reopened.

The patient was transferred to this hospital in January 1947. Physical examination revealed fairly good general condition, and the abnormalities noted above. Sputum was positive for tubercle bacilli on direct smear. Chest roentgenogram showed irregular honeycombing in the collapsed portion of the left upper lung with a slitlike cavity at the level of the left clavicle. There were fibrous markings of the left base and right lung. Pus from the sinus was negative for acid-fast bacilli. The length of the sinus tract was approximately  $1\frac{1}{2}$  inches, and it ended blindly in the thoracoplasty plaque.

After the sinus healed a two-stage revision thoracoplasty with apicolysis was performed and increased collapse was obtained. In doing the apicolysis, the cavity was incised. It was phenolized and closed with interrupted mattress sutures. Streptomycin, 2 gm. every day, was given for one month postoperatively. Three months after the operation the patient developed a broncho-extrapleural-cutaneous fistula. Both the sputum and secretions from the fistula were positive for acid-fast bacilli. The extrapleural space was deroofed.

In August 1947 a left upper lobe lobectomy was performed through an anterior incision. The internal orifice of the extrapleural sinus was closed. Streptomycin, 1 gm. per day, was given for one week before and two weeks after operation. On the fifth postoperative day the patient developed signs of thrombophlebitis and phlebothrombosis. A bilateral femoral ligation was performed, and subsequent recovery was uncomplicated.

Intrapleural aspirations yielded a small amount of fluid for about one week after resection. Streptomycin, 1 gm., was replaced after each tap. Granulation tissue obliterated the extrapleural sinus. The patient is clinically well and has a negative sputum.

*Operative Rationale.*—Pneumothorax, thoracoplasty and revision thoracoplasty failed to close the offending parenchymal cavities and led to sinus and fistula formation. The cavity and fistula were draining positive secretions into the bronchi and the extrapleural space, perpetuating the disease at both sites. Resection and streptomycin offered an approach for the control of the disease and its complications.

**CASE VIII (R. F., No. 20,087)\***—The patient is a 25 year old white married male. He was discharged from the service for psychoneurosis. Symptoms of

\* Since this manuscript was submitted the following significant developments have been observed in this patient: (a) the streptomycin sensitivity studies performed on the tubercle bacillus obtained from sputum prior to operation have been completed and show the organism to be streptomycin resistant. In effect, then, a segmental resection was performed without the protection of streptomycin, (b) there is radiographic evidence of active paren-

pulmonary tuberculousis dated to January 1944. These were cough, fatigability and weight loss. Roentgenograms were first taken in October 1945.

He was admitted to this hospital in February 1946. Treatment in addition to bed rest included right phreniclasia and pneumoperitoneum. The latter was discontinued after eight months as ineffective. The patient left the hospital against medical advice in January 1947. He was readmitted ten months later.

A review of the family history revealed that the patient's 2½ year old son had osseous tuberculosis.

Physical abnormalities on admission were limited to the chest and were the signs of right upper lobe cavitation. Sputum was positive for acid-fast bacilli on direct smear. The chest roentgenogram on admission showed a large, irregular paravertebral cavity in the right upper lobe between the first rib and the second intercostal space. By comparison with previous films this represented increasing excavation. Bronchoscopy showed no endobronchial disease.

Right upper lobe lobectomy was performed November 1947. The apex was found to be extremely nodular, fibrotic and contracted. Several visceral tubercles were present. The right middle and right lower lobes were nodular and over-expanded. The lung was densely adherent to the chest wall, and much of the dissection was done in an extrapleural plane to avoid rupture of the cavity. No fissure could be developed between the right upper and middle lobes. Following ligation of the hilar structures, these lobes were separated in segmental fashion. This necessitated dissection through diseased tissue showing caseation. Streptomycin, 1 gm. every day, was given one week before and two weeks after operation, and 1 gm. was injected intrapleurally three times per week. After two weeks there was essentially no pleural fluid.

Thoracoplasty was performed one month later with removal of ribs two to five.

The patient is clinically well and his sputum is negative. He has no evidence of empyema nor active pulmonary tuberculosis (Figs 428, 429 and 430).

*Operative Rationale.*—A giant cavity in the paravertebral gutter is often an indication for resection. Pneumothorax was thought to be dangerous with the giant peripheral cavity. Thoracoplasty often fails to close large paravertebral cavities. Psychiatric instability and previous discharge against medical advice gave support for the treatment of this patient without stage operation.

**CASE IX (R. K., No. 19,811)**—The patient is a 37 year old white single male. The onset of chest disease was in 1945 with "pneumonia." Subsequent roentgenograms in July 1945 and February 1946 were negative, but fatigability and nocturnal cough were prominent symptoms during this time. In March 1947 a chest roentgenogram revealed honeycombed infiltrations from the third intercostal space to apex on right.

chymal tuberculosis under the cleavage plane of the resection, (c) tuberculous wound infection became evident six months after operation; (d) inquiry into previous possible exposure to streptomycin revealed that the patient worked with streptomycin during the early phase of his disease.

Fig 428



Fig 429



Fig 430

Fig 428 (Case VIII) —A preoperative chest roentgenogram showing a giant cavity in the upper lobe of the right lung

Fig 429 (Case VIII) —A photograph of the resected upper lobe of the right lung showing giant excavation and nodular tuberculous foci

Fig 430 (Case VIII) —A photomicrograph of a histologic section from the surgical incision through caseous tuberculous tissue. In the lower right hand corner there is caseation. In the zones lying above this field may be seen fibrous and monocytic infiltration with histiocytes and lymphocytes. At 12 o'clock is a giant-cell surrounded by congested pulmonary parenchyma.

The patient's family history is significant in that a niece with whom the patient was living has developed tuberculous meningitis.

The patient was admitted to this hospital in May 1947. The only significant physical abnormalities were the signs of right upper lobe consolidation with many fine crepitant rales. Sputum was positive for acid-fast bacilli on direct smear.

The patient was placed on strict bed rest. Bronchoscopy showed tuberculous endobronchial disease with narrowing of the right upper lobe orifice. Serial roentgenograms revealed increasing disease. Right artificial pneumothorax was begun in July 1947, and good collapse was obtained. The right upper lobe became atelectatic and showed a 3 cm. cavity which rapidly increased in size during subsequent observation. The pneumothorax was diminished to a marginal space, and the collapse became selective for the right upper lobe which showed atelectasis and tension cavities. Streptomycin was begun for the endobronchial disease in a dose of 2 gm. per day as multiple injections every four hours. The endobronchial disease improved by bronchoscopy.

After sixty days of streptomycin therapy, the patient still had stenosis of the right upper lobe bronchus and open cavities. The remainder of the lung fields was stable.

Right upper lobe lobectomy was performed in December 1947. The postoperative recovery was uneventful. The patient is clinically well, and his sputum is negative on smear of a seventy-two hour concentrate. (Figs. 431 and 432.)

*Operative Rationale.*—Bronchial stenosis and tension cavities became pronounced after the induction of pneumothorax. Pneumonolysis, variation in the pneumothorax space, and intravenous atropine did not diminish the size of the cavities. Streptomycin improved the endobronchial disease but did not relieve the bronchial stenosis. No other parenchyma showed active disease. These factors made resection rational therapy.

**CASE X (P. L., No. 19,975)**—The patient is a 58 year old white married male. The symptomatic onset of his disease was in January 1946 with chest pain. A chest roentgenogram three months later showed an "infiltrate" in the left mid-lung field. After fifteen months he was hospitalized for "tuberculosis with a lung abscess." Numerous bronchoscopies were negative. Bronchoscopic lavage was positive for acid-fast bacilli on one occasion. He was treated with left phrenicectomy and pneumoperitoneum.

The patient was transferred to this hospital in August 1947. The positive sputum could not be verified, although he raised copious amounts of rather foul sputum. Chest roentgenogram showed a large cavity with a fluid level. The interpretation of the roentgenograms was: "The picture is not characteristic of pulmonary tuberculosis. One must consider a lung abscess probably secondary to tumor." Bronchoscopy was negative.

A left pneumonectomy was performed. A bronchogenic carcinoma with distal cavitation was found. Metastases to the hilar lymph nodes was noted on the pathological report. (Figs. 433 and 434.)



*Operative Rationale*—The diagnosis of pulmonary tuberculosis could not be established at this hospital. The confirmation of positive sputum

Fig 431

Fig 432

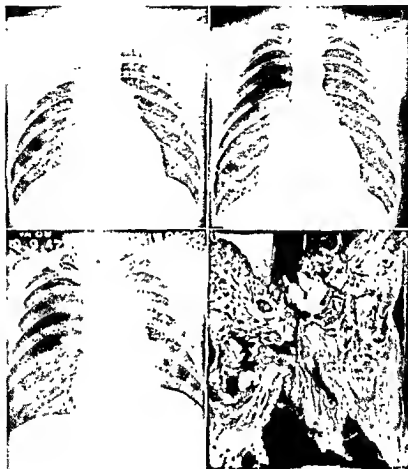


Fig 433

Fig 434

Fig 431 (Case IX)—A precollapse chest roentgenogram showing tuberculous infiltration and honeycombing of the right upper lobe

Fig 432 (Case IX)—A chest roentgenogram showing right pneumothorax with atelectasis and open cavities in the upper lobe of the right lung

Fig 433 (Case X)—A preoperative chest roentgenogram showing a large excavation in the left midlung field and the lateral margin of a hilar mass encroaching into the lumen

Fig 434 (Case X)—A photograph of the resected left lung showing a neoplastic abscess

should have been possible with such advanced disease. The history of twenty months' duration, negative bronchoscopies, negative Papani-

colaou smears, and the absence of enlarged regional lymph nodes were evidence against cancer. The roentgenogram and other factors, however, supported neoplasm as the most likely diagnosis. Thoracotomy was an absolute obligation. Pneumonectomy was therapeutic.

### COMMENT

The experience with the use of streptomycin for resection in this hospital is of fourteen months' duration. In pulmonary tuberculosis this report must be considered a preliminary one. Early experience is not always supported by later knowledge and accumulated observations; however, opinion must be formulated from current knowledge. The use of streptomycin has been observed closely and critically. An earnest attempt has been made to evaluate its effects from the experience to date. Some of the impressions outlined have been elaborated through the use of streptomycin in nearly 150 surgical and medical cases not subjected to resection and, therefore, they are perhaps justified in spite of the small number of cases recorded here.<sup>6</sup>

Streptomycin seems to support extirpative therapy. Its influence is most valuable during the surgical course of the case. The benefit during surgery is thought to be by prevention and suppression, not cure. The reactivation of previously stable disease during the acute surgical period seems to be suppressed. Bronchogenic, intrapleural and wound contamination are less bazarious. Their incidence is a function of mechanical factors and surgical technic; but the morbidity of clinical tuberculous spread, empyema and fistulas is reduced by streptomycin.

The use of streptomycin to prepare a patient for surgery must be judicious. Streptomycin-resistant strains of the tubercle bacillus developed in a significant number of patients.<sup>7</sup> This factor is thought to begin in about thirty-five days and to be complete in 70 per cent of patients after 120 days of continuous treatment. The initial in vitro sensitivity of susceptible strains was between 1 and 3 micrograms per 100 ml. The blood levels obtained by the dose given these patients were between 5 and 20 micrograms. Resistance may be from accommodation of the tubercle bacillus to streptomycin or from the proliferation of inherently resistant strains.<sup>8</sup> Extirpative surgery should be done before resistance occurs. Because of the time required to determine individual strain sensitivity it is usually necessary to proceed with therapy before the results of this test are available. While the routine use of streptomycin is not recommended for surgical collapse, all patients treated by resection should have the benefit of streptomycin.

Intrapulmonary and extrapulmonary contamination must be considered constant factors in lung resection for tuberculosis. The extracellular and most vulnerable period of the invading organisms is of short duration.

*Operative Rationale.*—The diagnosis of pulmonary tuberculosis could not be established at this hospital. The confirmation of positive sputum

Fig 431

Fig 432

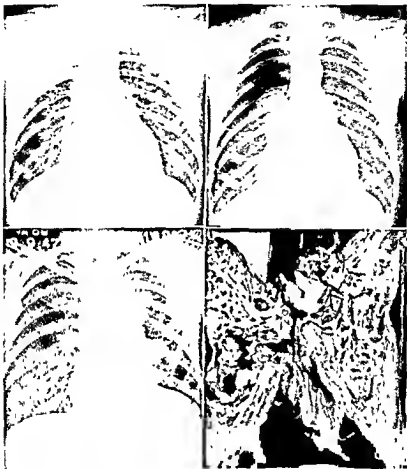


Fig 433

Fig 434

Fig 431 (Case IX) —A precollapse chest roentgenogram showing tuberculous infiltration and honeycombing of the right upper lobe

Fig 432 (Case IX) —A chest roentgenogram showing right pneumothorax with atelectasis and open cavities in the upper lobe of the right lung

Fig 433 (Case X) —A preoperative chest roentgenogram showing a large excavation in the left midlung field and the lateral margin of a hilar mass encroaching into the lumen

Fig 434 (Case X) —A photograph of the resected left lung showing a neoplastic abscess

should have been possible with such advanced disease. The history of twenty months' duration, negative bronchoscopies, negative Papani-

tuberculosis, since tuberculous parenchyma, lymphatics and bronchi are incised. The degree of contamination depends on the extent of the disease and the technic of excision. Resultant tuberculous empyema is a complication of significance.

In one patient (A. M.), a cavity wall invaded the parietes, and it was necessary to leave the wall in situ. This residual tuberculous tissue was thoroughly cauterized with 95 per cent phenol. Streptomycin was given intrapleurally only, in doses of 0.5 to 1 gm every other day for two weeks, and then two to three times per week for four weeks. Empyema did not develop. When streptomycin was not used in four cases of cavitory rupture reported by Bailey,<sup>12</sup> tuberculous empyema developed three times. In resection after thoracoplasty, cavitory rupture is more common. Bailey reported a ratio of 11:1 with an incidence of 60 per cent in post-thoracoplasty resection. However, better long-term results are claimed by some for lobectomy after thoracoplasty than when extirpation is performed under a thoracoplasty. In certain instances it may be wise to proceed with thoracoplasty before resection even though collapse failure is likely. This is done to reduce the amount of sputum, and to give trial to a more conventional therapy than resection.

The pleural space was grossly contaminated in one other patient (R. F.). It was necessary to create an artificial fissure through grossly diseased and caseous tuberculous tissue (Fig. 429). The patient received both intrapleural and intramuscular streptomycin. No empyema has developed. Under similar circumstances Sweet<sup>11</sup> and others elected to do pneumonectomy in preference to separating a lobe through diseased tissue. Sweet assigns the development of tuberculous empyema in two cases to the contamination from cutting across tuberculous lesions. He did not use streptomycin and did not do prophylactic thoracoplasty. Tuberculous empyema was reported by Overholt<sup>14</sup> in 72 per cent of 69 recent pneumonectomies for tuberculosis. Streptomycin was not used. Some patients had thoracoplasty performed. Bailey<sup>12</sup> has recorded the observation that pleural fluid often contains acid-fast bacilli without the development of tuberculous empyema if the space is rapidly obliterated.

Observations on intrapleural contamination have been stressed because it is believed that streptomycin is a valuable adjunct in the prevention of tuberculous empyema. The contaminating organisms in the pleural space are extracellular during the early postoperative period. This renders them readily accessible to antibiotic therapy. Intramuscular administration is supplemented with intrapleural instillations to obtain higher local concentration of streptomycin. Other measures are also used prophylactically. Phenolization of grossly diseased tissue may eradicate a main source of intrapleural contamination. Thoracoplasty is extremely

important and should be performed soon after recovery from the original operation. Its functions are at least two-fold: (1) obliteration of the intrapleural dead space to decrease the possibility of developing late empyema, and (2) prevention of overdilatation of the remaining parenchyma to suppress tuberculous reactivation and avoid the development of emphysema. Obliteration of the intrapleural space by the expansion of remaining pulmonary tissue seems hazardous. Resultant reactivation of tuberculous foci must be a factor in the recurrence of active pulmonary tuberculosis. In Overholt's cases<sup>15</sup> 50 per cent of those without collapse had ipsilateral spread within two years as compared to 16 per cent after thoracoplasty.

Thoracoplasty after resection is safer than when it is instituted as primary therapy. The major pathological process has been removed and paradoxical respiration and respiratory embarrassment are less; therefore, spread and reactivation can be expected to have a lower incidence. The type of thoracoplasty done is less shocking than a standard one, and it is not deforming since the first rib and the transverse vertebral processes are not excised.

It is felt that streptomycin with the other procedures outlined may contribute toward improving the results of extirpative treatment.

One other factor has been impressive in these cases when the pathologic specimens have been examined. These specimens show that useful pulmonary tissue has always been removed. It is not implied that this tissue is free from disease. It is nodular to palpation and microscopically may show foci of giant-cell reaction, but there can be no doubt that it was functional parenchyma. The lobes remaining within the thorax were also frequently nodular to palpation or showed disease by gross inspection. It is reasonable to assume that the contralateral lung may show similar involvement. Even though abnormal, this tissue represents the patient's pulmonary capacity and pulmonary reserve. Resection appreciably diminishes the pulmonary parenchyma and the added burden placed on the remaining lobes may be sufficient to cause reactivation of diseased foci.

From the series reported in the literature the over-all pneumonectomy death rate is approximately double that of lobectomy. The majority of deaths in both groups is late—more than sixty days after operation. Death in most cases was due to the recurrence of tuberculosis. In general, it must be presumed that the original disease was more advanced in patients requiring pneumonectomy but in addition it may be assumed that more useful pulmonary parenchyma was removed by pneumonectomy than by lobectomy.

The technic of segmental resection is well known. In tuberculosis it

has been avoided because the incision of tuberculous tissue has seemed dangerous. However, experience has shown the futility of attempting complete extirpation of the tuberculous process and elicited the danger of removing functional lung tissue in tuberculosis. Streptomycin and other measures have diminished the danger of localized excision. These data are complementary in suggesting a rational basis for segmental resection.

### SUMMARY AND CONCLUSIONS

1. Nine cases of pulmonary tuberculosis treated by resection and streptomycin are presented.

2. Streptomycin is a valuable adjunct to extirpative surgery in pulmonary tuberculosis.

3. It is believed that streptomycin will reduce the complications from intrapulmonary and extrapulmonary contamination with tubercle bacilli during surgical manipulation.

4. Streptomycin may inhibit the reactivation of quiescent pulmonary tuberculosis in unresected areas during and immediately following surgery.

5. During the protective period of streptomycin administration, selective thoracoplasty is performed to prevent late complication by empyema and reactivation from overdistention of diseased pulmonary tissue.

6. Lobectomy and pneumonectomy specimens in this series show that useful pulmonary tissue was excised. The conservation of useful parenchyma by segmental resection should improve the results of extirpative surgery in pulmonary tuberculosis. It appears that streptomycin may permit the safe surgical division of diseased pulmonary parenchyma incident to segmental resection.

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## THE USE OF STREPTOMYCIN IN PULMONARY RESECTIONS

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In January, 1947, the Veterans Administration Hospital at Oteen, North Carolina, was invited to participate in a cooperative study to evaluate the protective action of streptomycin in thoracoplasties and pulmonary resections for tuberculosis. The aim of this study was to determine whether streptomycin prevented or diminished the number of spreads or reactivations, empyemas and bronchopleural fistulas which often accompanied such operations and whether the prohibitive mortality rate formerly associated with resection could be reduced by its use. Since the study was initiated, sixty-three patients at the Oteen Hospital who have undergone either a lobectomy or a pneumonectomy for pulmonary tuberculosis have had streptomycin protection.

The dosage of streptomycin was 2 gm. daily, intramuscularly, until October 15, 1947, at which time it was changed to 1 grm daily, divided into two doses at twelve-hour intervals. The drug is given for one week preoperatively and two weeks postoperatively.

### HISTORICAL NOTES

The first scientific attempts at pulmonary resection were made on animals by Gluck,<sup>1, 2</sup> Schmid,<sup>3, 4</sup> Ziino,<sup>5</sup> Minreus,<sup>6</sup> and Biondi<sup>7</sup> in 1891-1893. Block<sup>8</sup> in 1881 attempted the first resection for tuberculosis on a living patient. He is reported to have done a bilateral, apical resection on a kinswoman who died during the operation. Soon afterwards he was driven to suicide by the legal complications arising from the ill-fated attempt. In the next few years unsuccessful efforts at pulmonary resection were reported by Kroenlein<sup>9</sup> and Ruggi.<sup>10</sup> In 1891 Tuffier<sup>11</sup> performed the first reported successful resection for pulmonary tuberculosis. These reports were followed by others including Lowson<sup>12</sup> (1893) and Doyen<sup>13</sup> (1895). From 1895 to 1933 many efforts to perfect a safe and successful technic for pulmonary resection were reported. These efforts were culminated in 1933 by the nearly simultaneous reports of successful resections by Lilienthal,<sup>14</sup> Graham,<sup>15</sup> Freedlander<sup>16</sup> and Rienhoff.<sup>17</sup> The

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mortality rate has remained high, however, and the morbidity accompanying the procedure has been discouraging. In 1942 Thornton and Adams<sup>15</sup> reviewed the literature and found twenty-nine reported pneumonectomies for tuberculosis with a mortality rate of 46 per cent and fifty-one lobectomies with a mortality rate of 25 per cent.

In reviewing the literature up to May, 1948, we were able to find 577 resections for tuberculosis with an over-all mortality rate of 26 per cent. The cases were followed from several months to eighteen years. The immediate operative mortality in these cases was 17 per cent.

### THE DESIRABILITY OF RESECTIONS

Maier<sup>13</sup> in 1945 considered resection for tuberculosis appealing but extremely hazardous and unwise. Gluck,<sup>1, 2</sup> however, as early as 1881 stated, "Surgeons must get used to the idea that resection of a portion of the lung may be an operative eventuality in some cases, but what mighty prejudices must be overcome!"

A physician who treats tuberculosis is often discouraged at the large number of patients who return to him with a progression of the disease several years after an apparent arrest has been obtained with the orthodox forms of therapy. The idea of excising the diseased focus as one would a malignant tumor, therefore, appeals to the surgical mind.

The previously reported high operative mortality, morbidity, and frequency of late complications, however, have discouraged too widespread an application of this radical surgical approach. Among the most frequent complications have been postoperative spreads or reactivations, empyemas, bronchopleural fistulas and wound infections. If these dread complications could be diminished to a safe point, pulmonary resection for tuberculosis would soon become an established procedure.

The discovery of streptomycin by Waksman<sup>20</sup> and others in 1944 has placed in our hands an agent whose bacteriostatic action against the tubercle bacillus has brought us a step nearer to this goal. Thoracoplasty remains the operation of choice in the majority of patients whose lesion has resisted, or is unsuitable for the lesser collapse measures. There will always remain, however, a number of patients with tuberculous bronchiectasis, residual cavities, tuberculomas, lower lobe tension cavities and the like whose disease cannot be controlled with a thoracoplasty. Until the ideal chemotherapeutic agent is discovered, we can offer these patients some hope by employing pulmonary resection protected with streptomycin.

During the past five years improvements in pre- and postoperative care, surgical technic and anesthesia have been rapid and numerous. Blalock<sup>21</sup> has added much to our knowledge of fluid balance. The use of

large amounts of blood for replacement and to combat shock was a development of the final years of the recent war. The early enthusiasm for plasma and synthetic blood substitutes faded when whole blood in sufficient quantities became available. Spies<sup>22</sup> and Youmans<sup>23</sup> contributed valuable work on vitamins.

Under improvements in operative technic may be listed the individual ligation of the vessels and secure closure of the bronchus. The use of the Overholt<sup>24</sup> prone position combined with skillfully administered anesthesia has lessened the possibility of postoperative spread. The closed circle anesthesia technic was introduced by Sword<sup>25</sup> in 1928. With cyclopropane and ethylene administered by a medical anesthesiologist experienced in thoracic surgery, the plane of anesthesia is so controlled that patients have usually regained consciousness by the time they are returned to their rooms. The early return of the cough reflex insures complete cleansing of the tracheobronchial tree early in the postoperative course. The diligence of the anesthesiologist in removing secretions by catheter suction during the operation is rewarded by a decreased necessity for postoperative bronchoscopic cleansing to combat atelectasis.

### INDICATIONS

The indications we have used for pulmonary resection for tuberculosis, and their relative frequency, are as follows:

1. Residual cavity after thoracoplasty—45 per cent.
2. Destroyed lung—12 per cent.
3. Failure of so-called conservative methods of collapse—15 per cent.
4. Tuberculoma—1 case.
5. Severe endobronchial disease and bronchiectasis—19 per cent.
6. Elective operations in place of thoracoplasty in unilobar cavitation—8 per cent.

### PROCEDURES

Since the initiation of the streptomycin study, all operations have been done in the Overholt prone position on the Albee-Comper table as modified by Murphy and Sword.<sup>26</sup> Anesthesia is induced with cyclopropane, ethylene and oxygen with the patient supine. After induction, a 15 gauge needle is inserted and securely fixed in an ankle vein in each leg. The Magill intratracheal catheter is then inserted and the patient placed in the prone position.

The sixth rib is resected from the transverse process to the midaxillary line. A 1 cm. section of the fifth and seventh ribs, just lateral to the process, is removed. The fifth, sixth and seventh intercostal nerves are crushed near the midline. We have found that it is easier to get the

patient to cough in the postoperative period because pain is diminished following crushing of the nerves. The pleural cavity is entered in the bed of the sixth rib, and by sharp dissection, sometimes aided by blunt dissection in the extrapleural plane, adhesions are separated and the lung freed. In patients who have had a thoracoplasty the incision and dissection do not follow any orthodox pattern. With Bethune rib shears the regenerated ribs and muscle bundles are divided parallel to and near the spine nearly to the cupola. Bleeding vessels are controlled with suture ligature. In separating the lung in this collapsed apical area it is not unusual to tear into the cavity and contaminate the pleura with its caseous contents. This is of course undesirable but as experience with the bacteriostatic action of streptomycin has accumulated we are less fearful of serious consequences.

The blood vessels are ligated with braided silk followed by a transfixion silk suture, clamped distally and divided. The bronchus is isolated as close to its division as possible, doubly clamped and divided. Two mattress silk sutures are placed proximal to the clamp and tied on the anterior surface of the bronchus. The ends of these sutures are left long. The clamp is removed and the end of the bronchus closed with several interrupted silk sutures. With the long ends of the mattress suture the posterior leaf of mediastinal pleura, or a flap of parietal pleura, is pulled over the end of the bronchial stump and fixed. A Pezzer catheter drain is placed in the dependent portion of the pleural space and left in place for forty-eight hours. The pleura is closed air-tight if a pneumonectomy is performed. In the case of a lobectomy an air-tight closure is not mandatory since it may be desirable to permit egress of air as the remaining lobe expands. The lung is expanded by positive pressure as the chest wall is closed. The drainage tube is connected to a suction machine permitting a negative pressure of 10 cm. of water in the lobectomies and to a simple water trap in the pneumonectomies.

The patient is usually awake with an active cough reflex at the end of the operation and seldom requires postoperative bronchoscopy. The additional anesthetic required to do a routine postoperative bronchoscopy

vs secretion period.  
blood is administered. Following the operation the patients lie on the operated side and are turned for a few minutes every two hours. The chest is supported manually once each hour during the first day and the patient forced to cough.

Six weeks after the resection a limited thoracoplasty is performed as described by Overholt,<sup>28</sup> leaving the first rib in place. We usually do not

do an anterior stage but are content with long segments of ribs removed through the posterior approach. The thoracoplasty prevents overdistention of the remaining pulmonary tissue and decreases the possibility of reactivation of small dormant foci of tuberculosis. In the case of lower lobe lobectomies, a phrenic nerve crush is done at operation or shortly thereafter. After a pulmonary resection, our patients are placed on bed rest for six months and then transferred for rehabilitation and vocational training. During the entire postoperative period an active program of muscle training and breathing exercises is supervised by the physiotherapy service to insure a minimum of deformity.

### RESULTS OF SURGERY

We have performed sixty-three resections at Oteen, using the above technique, with streptomycin as a prophylactic agent. The over-all sputum conversion rate has been 90 per cent. The sputum is negative in 92 per cent of all lobectomies performed and in 89 per cent of all pneumonectomies. In the surviving patients the sputum is negative in 95 per cent of the resections. We feel that this sputum conversion rate is remarkable, especially since only three patients had a negative sputum prior to surgery (Table 1). Our mortality rate is 5 per cent. These deaths have occurred within two weeks following the surgery. Two patients died of uncontrollable hemorrhage, one on the operating table and the other immediately on returning to his room. The third patient died several days after surgery of cerebral anoxia resulting from cardiac arrest due to hemorrhage at the operation. There have been no late deaths and all the patients are in excellent clinical condition and we do not expect any deaths in the near future.

Four empyemas developed as the result of a bronchopleural fistula. No empyemas developed unless a bronchopleural fistula was present. When we consider that during 25 per cent of all the operations the tuberculous cavity was torn into and still no empyemas resulted from this, we realize the tremendous bacteriostatic effect of the combination of penicillin and streptomycin. Only one spread has occurred during the entire series. This occurred in the contralateral lung of an uncooperative patient approximately one month after surgery. He did not develop a positive sputum. This so-called "spread" cleared in one month and the patient has been discharged from the hospital and is apparently well. We had two deep wound infections; both followed thoracoplasties which were performed six weeks after the resections. There have been no serious wound infections after the pulmonary resections.

The other complications in this series have been one meningitis, one pericarditis and the progression of the disease in one patient. The patient

TABLE 1  
RESULTS AT OPEN USING STREPTOMYCIN AS A PROPHYLACTIC

No of Patients	Early Deaths		Total Deaths		Emphysemas		Fistulas		Spreads and/or Exacerbations		Contra-lateral Disease Prior to Surgery		Wound-Infections		Other Complications		Neg Sputa		Per Cent Neg Sputa of Surviving Patients
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	
Lobectomy	1	2.8	1	2.8	1	2.8	1	2.8	1	2.8	11	31	0	0	2	5.0	33	92	94
Pneumonectomy	2	7	2	7	3	11	3	11	0	0	6	22	3	11	1	4	24	89	90
Total	3	5	3	5	4	6	4	6	1	1.6	17	27	3	5	3	5	57	90	95

with meningitis was treated with streptomycin and is apparently well. He has undergone a thoracoplasty since his meningitis cleared and is being discharged from the hospital. Pericarditis occurred in one patient. During a pneumonectomy we opened into the pericardial cavity. The pericarditis was clinically recognized approximately four weeks after operation. He has completely recovered and has been discharged from the hospital with an arrested status. The patient who developed a progression of his disease was readmitted to the hospital because of a cavity reopening in the contralateral lung sixteen months after surgery.

We feel that streptomycin has enabled us to obtain results which are difficult even for us to believe. We realize that these are early results since only 60 per cent have been completed more than six months. But the results with streptomycin are so much better than we were able to obtain prior to the use of streptomycin that we consider them remarkable.

During the first eight months of this study 2 gm. of streptomycin were given daily, one week before and two weeks after surgery. During the latter part of this study we have reduced the dosage to 1 gm. daily over a similar three-weeks' period. We have encountered no toxic effects from streptomycin, used only three weeks, with either the 2 gm. or the 1 gm. dose. Other studies in the Veterans Administration have shown that noticeable resistance occurs frequently after forty-two days' administration of streptomycin. We have encountered no resistant organisms from our three weeks' course.

Reviewing the literature we have been able to find 587 cases of pulmonary resections prior to the use of streptomycin (Table 2). In those cases where the results were reported we find a 17 per cent operative mortality and a 26 per cent over-all mortality. Empyemas developed in 20 per cent and fistulas occurred in 11 per cent of the resections. Spreads and/or exacerbations occurred in 26 per cent of all cases reported. The sputum conversion rate was 50 per cent.

There have been reported in the American literature (Table 3) 475 resections in which streptomycin was used as a protective agent.<sup>35, 44-52</sup> Among these patients, conversion of sputum was obtained in 78 per cent. Of the surviving patients the percentage was 86 per cent. The operations resulted in a total mortality rate of 9 per cent. Empyema developed in 4 per cent, fistula in three per cent and postoperative spread or exacerbation in 6 per cent.

We realize that factors other than streptomycin have contributed to the reduction in mortality and morbidity in our series. One of the most important of these has been the use of the Overholt position. One of us (J.A.M.),<sup>44</sup> operating at another hospital where the Overholt table was

TABLE 2  
 PLACEMARY RECTIONS REPORTED PRIOR TO USE OF STREPTOMYCIN

Authors	No. of Cases	Per Cent Deaths 1st Two Months	Per Cent Overall Deaths	Per Cent Emphysemas	Per Cent Fistulas	Spreads and/or Exacerbations	Per Cent Negative Sputa
Composite of Thornton, <sup>4</sup> Doherty <sup>25</sup> and Behrens <sup>26</sup>	83	6	40	50	30	20	Not completed
Overholt <sup>20</sup>	106	14	24	11	6	28	48
Bailey <sup>22</sup>	96	27	33	23	9	21	49
Sweet <sup>23</sup>	63	10	34	11	8	32	40
Jones <sup>24</sup>	84	0	10	19	13	16	Not reported
Clagett <sup>22</sup>	16	6	12	Not reported	Not reported	Not reported	Not reported
Strieder <sup>28</sup>	23	23	13	17	Not reported	Not reported	Not reported
Carr <sup>27</sup>	18	33	39	28	Not reported	Not reported	24
Moser <sup>8</sup>	16	6	6	13	6	23	73
Brantigan <sup>24</sup>	0	0	0	Not reported	Not reported	Not reported	Not reported
Churchill <sup>24</sup>	9	0	11	Not reported	Not reported	Not reported	Not reported
Kinsella <sup>9</sup>	6	33	33	53	33	16	50
Duncan <sup>9</sup>	5	0	0	0	0	0	100
Shenstone <sup>9</sup>	2	0	0	Not reported	Not reported	Not reported	Not reported
Moore, Murphy and Elrod <sup>14</sup>	11	18	36	55	33	27	35
Total	587	17	26	30	11	26	30

TABLE 3  
REPORTED RESECTIONS USING STREPTOMYCIN AS A PROPHYLACTIC AGENT

REPORTED INFECTIONS USING STREPTOMYCIN AS A THERAPY														
Surgeons	No. of Cases	Early Deaths		Late Deaths		Empyema		Fistula		Spreads and/or Exacerbations		Negative Sputa		Per Cent of Surviving Patients with Neg Sputa
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Cooperative Study of the V.A., Army and Navy <sup>18</sup>	129	5	4	6	5	5	4	8	6	4	3	96	74	78
Bailey <sup>18</sup>	100	10	10	16	16	3	3	4	4	1	1	77	77	92
Davidson <sup>17</sup>	59	Not reported		Not reported		Not reported		Not reported		5	8	Not reported		Not reported
Moody <sup>14</sup>	44	Not reported		Not reported		Not reported		Not reported		0	14	Not reported		
Haight <sup>19</sup>	41	0	0	0	0	Not reported		Not reported		2	5	Not reported		
Overholt <sup>10</sup>	40	4	10	4	10	2	5	0	0	2	5	Not reported		
O'Brien <sup>11</sup>	32	2	6	2	6	Not reported		Not reported		Not reported		Not reported		Not reported
Mulvihill <sup>12</sup>	31	0	0	0	0	0	0	2	6	1	3	31 <sup>13</sup>	100	
Moore (not performed at Otten, N.C.) <sup>14</sup>	14	3	21	3	21	0	0	0	0	2	14	10	72	
Clagett <sup>15</sup>	13	1	8	1	8	2	15	0	0	5	38	8	62	67
Total	475	31	8*	32	9*	12	4*	14	4*	28	6*	225	78*	80*

\* These percentages calculated from authors reporting these complications.



not available, encountered a rate of spread of 14 per cent. The same surgeon operating at Oteen using the prone position encountered a spread following only 1.6 per cent of operations.

### SUMMARY

A consecutive series of sixty-three patients have undergone pulmonary resection for tuberculosis. In this series streptomycin was used as a protective agent for one week preoperatively and two weeks postoperatively. By virtue of its protective action the mortality rate has been reduced from 26 per cent, as reported in the literature, to 5 per cent reported in this series. The incidence of empyema has been reduced from 20 per cent to 6 per cent and that of spread or exacerbation from 26 per cent to 1.6 per cent. The rate of conversion of sputum has been increased from 50 per cent to 90 per cent.

### CONCLUSIONS

The low mortality and morbidity rates following pulmonary resection for tuberculosis in which streptomycin is used as a protective agent are changing the concepts of surgery in tuberculosis. If the late results bear out the findings established by these early figures, the therapy of tuberculosis will be revolutionized.

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# AN EVALUATION OF STREPTOMYCIN AS A PROTECTIVE AGENT AGAINST SPREADS, REACTIVATIONS AND WOUND INFECTIONS FOLLOWING THORACOPLASTY FOR PULMONARY TUBERCULOSIS

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THE purpose of this report is to present the experience gained on the surgical service of the Veterans Administration Hospital, Oteen, North Carolina, as to the value of streptomycin as a protective agent against spreads or reactivations of disease, and against wound infections following thoracoplasty for pulmonary tuberculosis.

In the prestreptomycin era we performed 857 stages of thoracoplasty in 316 patients. This established one control group. In addition, another control group was established with our streptomycin study unit by the selection of alternate cases as controls. In the selection of cases as controls or as subjects for the use of streptomycin no partiality was shown as to the character of the disease, age of the patient, operative risk or other factors. Such random selection of cases gave a scientific cross section of the operative population. All cases receiving thoracoplasty were included in one or the other of the groups. The streptomycin-protected group consisted of forty-nine patients who were given 143 stages of thoracoplasty. Fifty patients had 128 stages without the use of this antibiotic agent.

## DOSAGE OF STREPTOMYCIN

During the streptomycin study period the dosage of the drug was reduced to obviate the untoward reactions that occurred with the original dose. The earlier dosages were 2.0 gm. and 1.8 gm. per day. With the 2.0 gm. dose, 0.4 gm. was given every four hours for five doses, one dose being omitted during the night. The 1.8 gm. dose was given every four hours in 0.3 gm. doses, the night dose being included. After several of the patients developed vestibular damage on these large doses the amount was reduced to 1.0 gm. per day and was administered in two 0.5 gm. doses. Thirty patients received the large doses of 2.0 gm. and 1.8 gm. per day, and nineteen patients received the 1.0 gm. per day dose. No clinical variations were noted with this reduction of dosage except for the re-

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*duction of vestibular complications* In all instances the drug therapy was instituted one week prior to surgery and was discontinued two weeks after the last stage of thoracoplasty.

### LABORATORY STUDIES

All cases receiving streptomycin were followed carefully by laboratory and roentgenologic studies. In the earlier members of the series blood counts, urinalyses and blood urea nitrogen determinations were made at frequent intervals to evaluate the effects which streptomycin might have upon the urinary and hemopoietic systems. As the study progressed the drug was found to exert no ill effects on these systems and the number of laboratory examinations were reduced. Roentgenographic examinations were made at weekly intervals during the course of the operative procedures and for one month after the last operative stage. Roentgenograms were then taken every month for the next six months. Caloric tests to evaluate vestibular function were performed prior to the institution of streptomycin therapy in each case and were repeated at the completion of the streptomycin therapy. In vitro streptomycin sensitivity tests were performed, using cultures of the organisms recovered from the individual cases, and it is of interest that in no case was the organism found to be significantly resistant to streptomycin prior to the administration of that drug. Audiograms were taken prior to, and following, streptomycin therapy.

### CHOICE OF ANESTHESIA

In the streptomycin study patients were anesthetized intratracheally through an intratracheal catheter. The patient was carried in the operating room under general anesthesia with minimum airway obstruction. Frequently during the operation a rubber catheter passed into the trachea for the restoration of the cough reflex. In the control group several anesthetic techniques were employed. In our present statistics are compared with the control group, all patients were anesthetized through an intratracheal catheter. The anesthetic was administered by the anesthesiologist to the surgical anesthesiologist. The surgical anesthesiologist performed the operation. The intratracheal catheter was removed at the termination of the operation.

At the onset of the study patients were followed carefully with a purely scientific approach. Streptomycin as a prophylactic against infections, and wound infection. The effectiveness of the drug was

sent our results as they were tabulated from the master sheets of our study unit file and will attempt to evaluate the efficacy of the drug from these statistics.

### RESULTS

**Prestreptomycin Group.**—In the 857 stages of thoracoplasty performed on 316 patients in the years prior to the advent of streptomycin there were twenty-eight spreads or reactivations. This is an incidence of 3.1 per cent spreads or reactivations per operation. As should be expected, the vast majority of the spreads, twenty out of the total of twenty-eight, occurred following the first stage of thoracoplasty; the remaining eight occurred after the second and third stages. Wound infections were found following twenty-four operations, or an incidence of 2.8 per cent.

A critical analysis of the follow-up data on this group of patients re-

TABLE 1  
PRESTREPTOMYCIN CONTROL GROUP

Patients	Thoraco- plasty Stages	Reactivations and Spreads		Wound Infections		Sputum Con- version and Cavity Closure		Deaths	
		No	%	No.	%	No	%	No	%
316	857	28	3.1	24	2.7	205	65.0	6	.75

veals that the sputum conversion rate is about 65 per cent. The mortality rate is about 0.75 per cent. The sputum conversion rate cited above is about the same as that obtained in other surgical clinics performing thoracoplasties upon patients with far advanced bilateral lesions. However, the mortality rate has compared favorably with that obtained in other clinics.

**Streptomycin Group.**—In 1947 the clinical study of streptomycin was instituted at Oteen, North Carolina, as well as in many other Veterans Administration hospitals. In our thoracoplasty series forty-nine patients underwent 143 stages of thoracoplasty with streptomycin as an adjunct in their therapy. Only one spread or reactivation occurred—an incidence of 0.7 per cent. There were two wound infections, or an incidence of 1.4 per cent. Thirty-two of these patients (65.3 per cent) converted their sputum and gained closure of their cavities. There were two deaths.

The control group consisted of fifty patients who underwent 128 stages of thoracoplasty without streptomycin as a prophylactic agent. In this group there were two spreads or reactivations (1.4 per cent). Wound in-

fections occurred in eight patients and sputum conversions were obtained in twenty-six patients. There were no deaths in this group.

**Evaluation of Results.**—In comparing the prestreptomycin and the streptomycin-treated patients it would appear that the percentage of spreads had been reduced from 3.1 per cent to 0.7 per cent by virtue of streptomycin protection. However, we believe that a number of other factors play important roles in this decrease. In the first place, many improvements in preoperative and postoperative care have been developed since 1943. In addition, in the prestreptomycin group the anesthesia was conducted by many different anesthesiologists employing many different techniques. In the streptomycin series, on the other hand, two anesthesiologists

TABLE 2  
STREPTOMYCIN STUDY GROUP

	Patients	Thoracoplasty Stages	Reactivations and Spreads		Wound Infections		Sputum Conversion and Cavity Closure		Deaths	
			No.	%	No.	%	No.	%	No.	%
Streptomycin Group	49	143	1	0.7	2	1.4	32	65.3	2*	4.1
Control Group	50	128	2	1.5	8	6.2	26	52.0	0	

\* One patient died from a brain abscess four weeks following his last stage of thoracoplasty. The other died of cardiac failure five weeks subsequent to his last thoracoplastic stage. Both patients refused to continue streptomycin therapy three weeks after the onset of therapy.

of considerable skill conducted the anesthesia, using cyclopropane and intubation in each case. In the study unit group there is no essential difference in the incidence of spreads or reactivations between the treated cases and the control cases.

Comparison of the incidence of wound infections shows definite advantage in the streptomycin-treated cases. Whereas only 1.4 per cent of the treated cases had wound infections, there was an incidence of 6.2 per cent wound infections in the control cases. However, if we again turn to the prestreptomycin series, the incidence of such wound infections is about 2.8 per cent. Therefore, it appears that the incidence of these infections is probably about the same.

In comparing the sputum conversions and cavity closure percentage between the control group and the streptomycin group it is found that a

larger percentage converted their sputum and closed their cavities in the streptomycin group. These figures represent early results and do not represent a true final evaluation of the series because many of the control group will convert their sputum in the months following the operative procedure and many of the streptomycin group will reconvert their sputum to positive after the effects of streptomycin are withdrawn.

We have yet to determine whether resistance *in vitro* actually means an equivalent resistance *in vivo*. If this true, then further treatment is useless when such resistance to streptomycin is present. In our series no streptomycin resistance occurred prior to the forty-fifth day of therapy with that drug. However, after the forty-fifth day resistance occurred with increasing frequency in direct proportion to the time that therapy was prolonged.

In conclusion, therefore, the protective action of streptomycin against spreads or reactivations and wound infections following thoracoplasty for pulmonary tuberculosis has not been definitely established in our series. Since the thoracoplastic procedures are performed for chronic cavitary and predominantly productive tuberculous lesions in patients who have demonstrated their resistance against the tubercle bacillus, and since our results show that the results of thoracoplasty are the same in both the streptomycin and control groups of the study unit, it would appear more logical to withhold streptomycin so that its effectiveness would be maximum if spreads or reactivations occurred. If the *in vivo* studies confirm the theory that streptomycin-sensitive strains of tubercle bacilli are replaced by streptomycin-resistant strains after the forty-fifth to sixtieth day of therapy, the use of this agent would be contraindicated in thoracoplasty cases.

#### SUMMARY

1. An evaluation of streptomycin as a protective agent against spreads, reactivations and wound infections occurring during thoracoplasty is made.

2. Statistics are given for both streptomycin study unit and control groups. Results are included for a prestreptomycin study group for comparison.

3. The value of streptomycin as a protective agent against the usual complications of thoracoplasty has not been impressive. It is our opinion that streptomycin should not be used for the routine thoracoplasty case but should be reserved for the treatment of complications as they arise.





## THE USE OF STREPTOMYCIN IN THORACOPLASTY FOR PULMONARY TUBERCULOSIS

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THE bronchogenic spread of tuberculosis and tuberculous wound infection are serious complications during and after thoracoplasty.

Not all roentgenographic densities appearing after thoracoplasty represent the bronchogenic spread of tuberculous disease. Such shadows may be those of nontuberculous pneumonia, atelectasis, pulmonary edema, the reactivation of tuberculosis, autotuberculinization, or hematogenous tuberculosis.<sup>1, 2</sup> In general, however, the shadows in the lower or contralateral lung fields seen in roentgenograms a few hours after a stage of thoracoplasty represent atelectasis that becomes bronchogenic spread of tuberculosis. The point at which postoperative atelectasis or consolidation becomes "spill" or "spread" of tuberculous disease cannot be sharply defined. The point at which this postoperative shadow represents nontuberculous pathologic processes, such as simple atelectasis or pneumonitis, can often be defined more sharply. Unfortunately, in the past, the lack of specific treatment provided time for the tragedies of mistaken diagnosis. In this clinic, all new postoperative radiographic densities of the pulmonary parenchyma are regarded as potential foci of exudative tuberculosis, and are treated with streptomycin, in conjunction with other established procedures. We have attempted to alter the course of this pulmonary density rather than classify it. The roentgenographic clearing of these pathologic processes may not always be due to streptomycin.

### SELECTION OF CASES

Under Veterans Administration protocol regulations, we employed streptomycin in alternate candidates for thoracoplasty. In other respects, identical clinical factors obtained for both series. The presence of endobronchial disease or previous streptomycin administration for medical treatment did not alter the classification of patients. Streptomycin calcium chloride in daily doses of 2 gm. was begun one week before the scheduled first stage of operation. This was divided into five injections of

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0.4 gm each every four hours. The 4 A.M. medication was omitted. This schedule was continued for two weeks after the last stage of thoracoplasty, and averaged sixty days of treatment.

From January 1947 to December 1947, eighteen thoracoplasty candidates met protocol requirements for inclusion in this study. Nine alternate patients were selected for streptomycin administration, while nine served as controls.

#### DETAILS OF OPERATIVE REGIMEN

In order to correlate our results with those from other Veterans Administration hospitals, the surgical conditions under which these patients were operated are reviewed.

Preoperatively, blood, vitamin, and protein supplements were given as indicated. Seventy-two hours before operation, aerosol and intramuscular penicillin were started.

Premedication included a barbiturate, morphine sulfate and scopolamine. Local and general anesthesia were used with equal frequency in both the control and streptomycin patients. No difference in postoperative complications attributed to the type of anesthesia was apparent. At operation, slight Trendelenburg incline was maintained. Under general anesthesia, endotracheal tube suction was utilized every ten minutes. If there were copious excretions, bronchoscopic aspiration was performed at the end of the operation. The patient was asked to cough and breathe deeply at frequent intervals when local anesthesia was used.

To reduce the postoperative discomfort, the first six intercostal nerves were resected. Below this level, infiltration of the nerve sheaths with nupercaine in oil provided some relief of postoperative pain.

The use of blood, nasal oxygen, infusions, pharyngotracheal aspirations, support to the operative site, mobilization from back to operative side, insistence on coughing, and portable chest roentgenogram is all part of the standard postoperative regimen.

#### CASE STUDY

**Streptomycin Cases.**—The nine patients receiving streptomycin had a total of twenty-nine stages, with an average of 2.5 ribs removed per stage. Conversion of sputum and cavity closure occurred in eight patients. Two operative complications occurred. There were no deaths.

The first complication was in a 25 year old Negro who developed an extra-pneural infection immediately after a third stage thoracoplasty. Incision and

Fig. 435

Fig. 436



Fig. 437

Fig. 438

Fig. 435 (E. Q., No. 19,077) —A chest roentgenogram taken before the second stage of thoracoplasty which shows a right apical cavity and the first stage of thoracoplasty.

Fig. 436 —A chest roentgenogram after the second stage of thoracoplasty which shows atelectasis of the right lower lobe and a collection of extrapleural fluid. This patient was aspirated bronchoscopically and given streptomycin therapy.

Fig. 437 —A chest roentgenogram before the third stage of thoracoplasty. There is a residuum of fresh exudative disease in the right lower lung field.

Fig. 438 —The present status of the patient. This shows the increase in right lower lobe disease four and one-half months after the third stage of thoracoplasty and four months following discontinuation of streptomycin. Drug fastness probably occurred during the thoracoplasty regime because of a four months course of streptomycin prior to the surgical program.

Fig. 439

Fig. 440

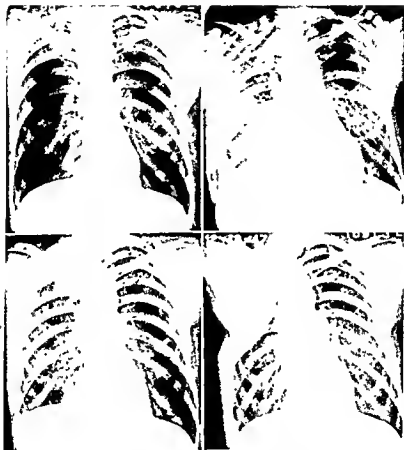


Fig. 441

Fig. 442

Fig. 439 (J V S, No 19,933).—The preoperative chest roentgenogram which shows right apical excavation

Fig. 440 —A portable chest roentgenogram eighteen hours after the first stage of thoracoplasty which reveals ipsilateral lower lobe and contralateral midlung density

Fig. 441 —A chest roentgenogram taken before the second stage of thoracoplasty which shows considerable roentgenographic clearing of the densities after fifteen days of streptomycin therapy

Fig. 442 —A chest roentgenogram of the patient three and one-half months after the completion of his thoracoplasty. No residual roentgenographic disease is evident in the area of previous postoperative pulmonary densities

granulations obliterated the sinus, and within forty-five days it was completely healed. One week later, streptomycin was discontinued.

Fig 443

Fig 444

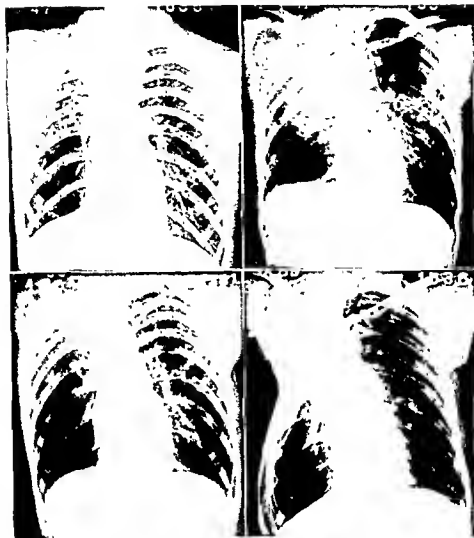


Fig 445

Fig 446

Fig 443 (H. F. A., No. 19,688) —The preoperative chest roentgenogram which shows right apical cavitation and atelectasis

Fig 444 —The chest roentgenogram eighteen hours after a first stage thoracoplasty which shows fresh bilateral infiltrations

Fig. 445 —A chest roentgenogram taken before the second stage of thoracoplasty which shows considerable clearing of the infiltrations after three weeks of streptomycin therapy.

Fig 446 —A chest roentgenogram two months after the completion of the thoracoplasty which shows increased linear markings in the area of previous infiltrations.

The second complication in this group occurred in a 30 year old white male. He had received 18 gm. of intramuscular streptomycin every day for four months

Fig 447

Fig 448



Fig 449

Fig 450

Fig 447 (J J C , No 19,029) —A chest roentgenogram taken before a third stage thoracoplasty which shows thoracoplastic collapse on the right side

Fig 448 —A chest roentgenogram taken after the third stage thoracoplasty which shows lobular consolidation in the left upper lobe

Fig 449 —A chest roentgenogram taken nine days after the third stage of thoracoplasty which shows considerable clearing of the lobular consolidation in the left upper lobe No streptomycin was given

Fig 450 —A chest roentgenogram of the patient nine months after the last stage of thoracoplasty This shows only increased linear markings in the area of previous consolidation This is stationary.

to combat contralateral exudative disease in preparation for thoracoplasty. At the second stage of operation (Fig. 435), this man developed atelectasis of the right lower lobe (Fig. 436). After bronchoscopy, the atelectasis cleared incompletely, and it was apparent during the next two weeks that there was a residuum of fresh exudative disease in the right lower lung field (Fig. 437). In spite of this, the third stage of thoracoplasty was performed essentially on schedule. Streptomycin was continued for two weeks after the third stage of operation and the spread remained unchanged. Following the omission of the drug, increasing disease was noted on serial roentgenograms (Fig. 438).

**Control Cases.**—Nine patients underwent thirty-one stages of thoracoplasty without preliminary streptomycin. There were no deaths and three operative complications. Two of these were treated with streptomycin. Cavity closure and sputum conversion occurred in eight patients.

The first complication followed the initial stage of thoracoplasty for right apical cavitation in a 51 year old white male (Fig. 439). His postoperative roentgenogram revealed ipsilateral lower lobe and contralateral midlung density (Fig. 440). There was moderate dyspnea, which was relieved by bronchoscopic aspiration. Because of his age, this patient was given only 1 gm. of streptomycin every day, beginning with the first postoperative day. Roentgenographic clearing began in three days, and the second stage of thoracoplasty was performed in two and one-half weeks (Fig. 441). No residual roentgenographic disease is evident in the area of the postoperative atelectasis four months after completion of surgery (Fig. 442).

The second complication occurred in a twenty-five year-old white male (Fig. 443), who developed bilateral infiltrative opacities following the first stage of thoracoplasty (Fig. 444). Bronchoscopy was effective. Streptomycin was administered in the usual 2 gm dose. Considerable clearing of these infiltrative areas occurred within two weeks, and the second stage of thoracoplasty was delayed but one week beyond the usual interval of two weeks (Fig. 445). Post-operative follow-up reveals increased linear markings in the area of previous infiltration (Fig. 446). This is now stationary.

Another patient in this group developed moderate contralateral lobular consolidation after his third stage of thoracoplasty (Figs. 447 and 448). After bronchoscopy, this area cleared considerably, and within nine days, only increased parenchymal markings remained (Fig. 449). No streptomycin was given. Nine months later these markings persist (Fig. 450).

#### COMMENT

Over 23,000 stages of thoracoplasty were performed on nearly 10,000 patients between 1937 and 1941.<sup>1</sup> There was a 22 per cent increase in the incidence of this operation during this period.<sup>2</sup> Seven to 12 per cent of



sanatorium admissions<sup>4, 5</sup> and 4 per cent of all tuberculous patients<sup>3</sup> undergo thoracoplasty. In various thoracoplasty series there is a 2 to 13 per cent patient mortality,<sup>6-21</sup> and from 18 to 33 per cent of early postoperative deaths are due to tuberculous spread or tuberculous pneumonia<sup>6, 8, 12, 13</sup>. Three to 18 per cent of thoracoplasty patients develop tuberculous spread,<sup>6, 8, 11, 14, 15</sup> and this carries its own hazard as well as the hazard of interrupting the original collapse program.

In our hospital, thoracoplasty was performed on nine patients receiving streptomycin and nine patients without preliminary streptomycin. One patient in the streptomycin group developed a tuberculous and staphylococcal extrapleural infection following a third-stage thoracoplasty. The operative sinus which followed incision and drainage of this mixed extrapleural infection healed within forty-five days. This is consistent with the experience of others in the management of tuberculous sinuses when streptomycin is used<sup>24, 25</sup>. Healing time could have been shortened by secondary closure. This point of secondary closure assumes greater importance if further stages of thoracoplasty become necessary. A second patient in the streptomycin group developed a postoperative tuberculous spread which remained stationary under drug therapy but progressed after the drug was discontinued. This patient may be presumed to have been rendered streptomycin fast by the administration of the drug for a period of four months before the surgical program was undertaken.

Three of the nine patients in the control group developed postoperative roentgenographic shadows of the pulmonary parenchyma. Two of the three received streptomycin for a potential exudative tuberculous lesion which would otherwise have prevented completion of their collapse program. Their pulmonary densities underwent progressive radiographic clearing. The areas of fresh postoperative infiltration did not develop into fibrocavernous pulmonary tuberculosis. In one patient these areas continued on to complete resolution. In a second patient, there remain increased lung markings which appear inactive. The third patient in this group did not receive streptomycin for his postoperative pulmonary density. He was watched as a control as his thoracoplasty had been completed. The roentgenologic pulmonary shadow of this patient resolved considerably in nine days. At present, increased lung markings remain in this area. This case demonstrates the difficulties encountered in evaluating a drug in the treatment of a disease complication so protean as tuberculous spread.

### CONCLUSIONS

1. Streptomycin has exerted a favorable influence on the behavior of a postoperative tuberculous wound infection.

2. The favorable effect of streptomycin in exudative pulmonary tuberculosis<sup>22, 23</sup> prompts us to institute streptomycin treatment immediately upon the roentgenological detection of atelectasis or consolidation following a stage of thoracoplasty. Vital time is not sacrificed to differentiate tuberculous from nontuberculous processes.

3. This experience is inadequate for conclusions as to the advisability of using streptomycin prophylactically during the thoracoplasty regimen. The impression has been gained, however, that if frequent roentgenograms are taken immediately after surgery, detection of potential spread can be early visualized and the administration of streptomycin can be instituted in time to abort the tuberculous infection.

4. Streptomycin permits continuation of the collapse program even in the presence of post-thoracoplasty pulmonary densities.

5. Streptomycin has been presented as a useful drug. Its use is constantly attended by the possibility of bacterial resistance. Therefore, the promiscuous use of the drug is to be avoided.

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# THE USE OF STREPTOMYCIN AND THORACOPLASTY IN THE POOR RISK PATIENT

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## INTRODUCTION

SINCE the early development of surgical technics in the treatment of pulmonary tuberculosis, surgeons have had to accept or reject poor risk patients whose only reasonable opportunity for survival has rested with thoracoplastic collapse. The line of definition between the "reasonable risk" and the "desperate risk" has fluctuated from place to place and time to time depending upon where emphasis is placed among the individual factors. Prime emphasis should center on the advantages and the disadvantages to such a patient as the result of the surgical procedure. Nevertheless the reputation of the surgeon and the public relations of the hospital often become component parts of the final resolution.

By general agreement, patients who have coinciding complications in addition to the standard pattern of thoracoplasty disease are called poor risks. These complications in different zones of the chest may require the gamut of supportive therapeutic procedures prior to and during the time of thoracoplasty. It has been apparent that surgical versatility, penicillin and chemotherapy were not enough to weight the balance in favor of these patients. A drug having an action specifically on the tubercle bacillus was needed to supplement our armamentarium. That streptomycin might be that drug appeared probable. With this in mind the following patients, who presented many specific contraindications, were selected for thoracoplastic collapse.

Of eight patients in our poor risk category, four had bronchopleural fistulas, two of these with mixed empyema; two had tension cavities, one had empyema and destruction of his right lung with a partial thoracoplasty on the contralateral side. The remaining one presented a large cavity with other disease in his right lung and excavation on his left side. He was running a toxic course when pneumothorax was instituted. Surgery was considered necessary before his pneumothorax became stabilized.

Most of these patients demanded immediate surgery.

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## ILLUSTRATIVE CASES

Three representative examples have been selected for presentation, five others have been summarized

**CASE I (P. C., No. 16870)**—A 22 year old white male was admitted July 3, 1947. He had had a left artificial pneumothorax induced October 1945 for cavitory disease. This procedure was ineffective and was abandoned three months later. At that time infiltrations had appeared in his right apex. On February 27, 1947, he suffered a spontaneous collapse of his left lung which resulted in a bronchopleural fistula with tuberculous empyema. In January 1947



Fig. 451



Fig. 452

**Fig. 451 (Case I)**—The left lung is 50 per cent collapsed. The intercostal tube is shown at the base of the left empyema cavity. Midzonal fibronodular disease is seen on the right.

**Fig. 452 (Case I)**—A nine rib left thoracoplasty has been completed and the intercostal tube removed. The right lung has remained stable.

there developed a pleurocutaneous fistula on the left at the level of the eighth interspace in the posterior axillary line.

On admission to the hospital, the patient was toxic and extremely debilitated. The pleurocutaneous sinus was positive on smear for tubercle bacilli. Bronchoscopy revealed active bilateral endobronchial disease. Chest x-rays revealed midzonal fibronodular disease on the right (Fig. 451), and a partially collapsed left lung (50 per cent). Under this collapse a giant cavitory lesion could be seen in the apex extending to the lower third of the lung. The patient was started on a 120 day course of streptomycin by the intramuscular route. The dose was 2 gm. daily. His sinus tract was excised and an intercostal tube inserted into the empyema space. Continuous suction was employed.

On August 12, 1947, a nine rib left thoracoplasty in six stages was started. The intercostal tube was removed immediately after the last stage, and the sinus tract closed spontaneously (Fig. 452). An extrapleural pocket, which followed the fourth stage of thoracoplasty, was infected with staphylococcus albus (coagulase-positive). This healed rapidly with drainage, moist heat and penicillin.

At present, the patient's clinical condition is much improved. His sputum is negative and chest x-rays reveal satisfactory thoracoplasty collapse. His right lung is stable.

#### SUMMARY

- Problem:*
1. Marked debilitation
  2. Bilateral parenchymal disease
  3. Large cavity, left apex
  4. Bronchopleural fistula and empyema, left
  5. Pleurocutaneous sinus, left
  6. Bilateral endobronchial disease

- Treatment:*
1. Streptomycin
  2. Excision of sinus tract
  3. Suction drainage for empyema
  4. Extensive multistage thoracoplasty

*Comment.*—A contemplated Schede thoracoplasty was avoided. The endobronchial disease showed marked clearing; only scars remain in its place. The intercostal tube sinus healed spontaneously.

#### CASE II (M. H., No. 16894)

#### SUMMARY

- Problem:*
1. Debilitation and septic course
  2. Bronchopleural fistula of right lung
  3. Pleurocutaneous sinus of right chest
  4. Empyema, right base
  5. Infiltration in left midlung field

- Treatment:*
1. Streptomycin, 1 gm. daily
  2. Open right anterior stage thoracoplasty
  3. Thoracotomy for empyema drainage
  4. Eight rib right thoracoplasty in three posterior stages

*Comment.*—Contemplated Schede thoracoplasty was avoided. Sinuses closed spontaneously. Sputum converted. General condition good.

#### CASE III (A. O., No. 16823)

## SUMMARY

- Problem:*
- 1 Debilitation
  - 2 Copious sputum
  - 3 Cavitation at right apex
  - 4 Bronchopleural fistula of left lung
  - 5 Empyema, left base

- Treatment:*
- 1 Streptomycin, 2 gm daily for 120 days
  - 2 Intercostal tube with constant suction for empyema drainage
  - 3 Left anterior stage thoracoplasty

*Comment*—This patient had had psychiatric disturbances prior to admission. After his anterior stage thoracoplasty, he became unmanageable and surgical procedures were abandoned. All wounds healed. He still has cavitation at his right apex and a cold hydropneumothorax at his left base. He has gained 18 pounds and has only 2 ounces of sputum daily.

## CASE IV (A P, No 13226)

## SUMMARY

- Problem*
- 1 Bronchopleural fistula and empyema, left chest
  - 2 Unstable disease in right lung, unsuccessfully treated with pneumothorax
  - 3 Toxic and debilitated

- Treatment*
- 1 Streptomycin, 2 gm daily for 120 days
  - 2 Intercostal tubes with constant suction for empyema drainage
  - 3 Left posterolateral thoracoplasty consisting of eight ribs in five stages

*Comment.*—Attempts to expand the left lung by suction failed. The bronchopleural fistula closed prior to thoracoplasty. A contemplated Schede thoracoplasty was avoided. The tube sinuses are still patent but show evidence of closing. The sputum is negative and x-rays are stable.

CASE V (A K, No 16683) —An extremely debilitated 34 year old white male was admitted March 27, 1947, with a partial three rib thoracoplasty on the left, extensive cavitory disease throughout the upper two-thirds of the right lung and fluid at the right base. An eight rib right thoracoplasty in five stages was performed with streptomycin as an adjunct (18 gm daily from April 18 to July 30, 1947). There was no appreciable change in his vital capacity. His sputum was converted, x-rays remained stable and his clinical condition im-

antibiotic therapy. He did not recover from this episode and went on to develop a nonspecific left lower lobe pneumonia which failed to respond to treatment. He expired two days later in a peripheral vascular collapse. At autopsy, the left lower lobe was found to be consolidated and the remaining portion of the right lung collapsed and shrunken under the thoracoplasty. The left lingular segment comprised his total ventilatory tissue at the time of death. Meningococci were cultured from the consolidated lung.

#### SUMMARY

- Problem:*
1. Total destruction of right lung
  2. Empyema, right base
  3. Partial thoracoplasty on left
  4. Low pulmonary functional reserve

- Treatment:*
1. Streptomycin
  2. Oxygen and supportive therapy
  3. Extensive right thoracoplasty

*Comment.*—Conversion of sputum and reduction in its amount were effected. Although this patient remained a respiratory cripple, an extensive multistage collapse was completed with no significant change in his vital capacity.

**CASE VI (S. R., No 16848)**—This 24 year old, acutely ill Negro was admitted June 23, 1947, one week after the onset of blood-streaked sputum. He had known of his disease for one year previously but had chosen to remain at home. During that time, he became progressively debilitated. Admission chest films revealed an 11 by 7.5 cm apical cavity on the left, a considerable pleural haze over the entire left lung and a patchy infiltration of the right apex (Fig. 453). His pulse was 110, his temperature was 101°F, and his sputum was highly positive. Bronchoscopy revealed laryngotracheal tuberculosis as well as extensive nonstenosing disease of the left main stem bronchus.

Seven days prior to surgery, the patient was started on a course of intramuscular streptomycin consisting of 2 gm. daily. On July 10, 1947, he underwent a left anterior stage thoracoplasty preparatory to a Monaldi cavernostomy. On the second postoperative day he became dyspneic; roentgenogram revealed left lower lobe atelectasis. This was relieved by bronchoscopic aspiration. On July 22, 1947, a left Monaldi cavernostomy was performed and suction was started. The patient had a three stage, seven rib posterolateral thoracoplasty completed September 15, 1947 (Fig. 454).

On November 17, 1947, while the Monaldi sinus was being calibrated with lipiodol, the patient suffered an air embolus. Neurological sequelae cleared within several days but streptomycin was continued beyond the usual 120 days. The drug was given a total of 150 days during which time the Monaldi catheter was removed. The sinus tract closed spontaneously in 10 days. This patient left the hospital against advice because of problems at home. At that time his



clinical condition was good, his sputum was negative and his x-rays were stable (Fig. 455).

Fig 453



Fig 454



Fig 455

Fig 453 (Case VI) —Admission chest film reveals an 11 by 7.5 cm. cavity in the left apex. There is patchy infiltration in the right apex.

Fig 454 (Case VI) —A seven rib thoracoplasty has been completed. The Monaldi

sinus tract. This tract was closed at the time of discharge.

#### SUMMARY

- Problem:*
- 1 Extreme debilitation
  - 2 Left apical cavity and contralateral spread
  - 3 Laryngotracheal and extensive endobronchial disease

- Treatment:* 1. Streptomycin  
2. Monaldi cavernostomy with suction  
3 Seven rib thoracoplasty

*Comment.*—This patient was rendered sputum-negative. Parenchymal disease was stabilized. Since he left the hospital because of an emergency, determination of his endobronchial disease by bronchoscopy was not possible.

#### CASE VII (L. T., No. 13393)

##### SUMMARY

- Problem:* 1. Unsuccessful pneumothorax on the right side followed by empyema  
2. Tension cavity in right apex  
3. Fresh cavitary disease in left apex

- Treatment:* 1. Left pneumothorax  
2. Right anterior stage thoracoplasty  
3. Right Monaldi cavernostomy with constant suction drainage  
4. Intensive aspirations of empyema cavity  
5. Intrapleural streptomycin and penicillin  
6. Seven rib posterolateral thoracoplasty on right in three stages  
7. Streptomycin, 2 gm. daily for sixty days, following thoracoplasty

*Comment.*—The first anterior stage thoracoplasty was considered necessary before the left pneumothorax was stabilized. The patient's empyema has cleared and his Monaldi sinus has closed.

#### CASE VIII (F. D., No. 15946).

##### SUMMARY

- Problem:* 1. Large cavity in the right apex  
2. Small cavities with spreading disease in the left apex  
3 Progressive debilitation

- Treatment:* 1. Right phrenic crush and pneumoperitoneum  
2. Right intrapleural pneumothorax was unsuccessful  
3. Left intrapleural pneumothorax  
4. Right posterolateral thoracoplasty; seven ribs and partial scapulectomy in three stages  
5. Streptomycin, 2 gm. daily for sixty days

*Comment.*—Pneumoperitoneum was discontinued because it could not be tolerated by the patient. The right pneumothorax was unsuccessful

tralateral spread had become stabilized and the patient afebrile. The tuberculous effusion was repeatedly aspirated and the underlying lung

Fig 456

Fig 457

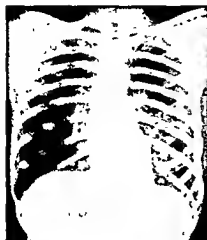


Fig 458

Fig 459

Fig 456 (R P, No 7) —Giant tension tuberculous cavity in left lower lobe

Fig 457 —Spontaneous left pneumothorax with collapse of giant cavity and contralateral pneumonic spread in right upper lobe

Fig 458 —Persistent left tuberculous empyema partially reexpanded cavity in left lower lobe and contralateral spread stabilized by streptomycin.

Fig 459 —Following completion of thoracoplasty with collapse of lower lobe cavity and empyema space

reexpanded, although by this time a tuberculous infiltration was present throughout the left lower lung. Following the completion of ninety days

of streptomycin with a total of 113 gm. the patient had a negative sputum and was considered suitable for a thoracoplasty. A five stage, eleven rib, left thoracoplasty was performed beginning on October 23, 1947, with the streptomycin continued throughout the procedure to a total of 313 gm. No complication occurred during or following the thoracoplasty and the patient has continued to gain weight and remained afebrile with a negative sputum until the present time, four and one half months post-operatively.

Another outstanding example of the benefit derived from streptomycin



Fig 460



Fig 461

Fig 460 (L D, No 1) — Extensive left parenchymal tuberculosis and mixed tuberculous empyema before drainage

Fig 461 (No 1) — After collapse by Schede thoracoplasty

is that of L. D. (No. 1, Figs. 460, 461) with a mixed tuberculous empyema and a daily temperature of 103° F. Although some of these patients survived a complete Schede thoracoplasty before antibiotics were available a high percentage never completed their proposed number of procedures. This 23 year old man with a two year history of tuberculosis was treated elsewhere by an ineffectual left pneumothorax which developed into a tuberculous empyema. A mixed empyema then occurred with multiple draining pleurocutaneous fistulas through needle tracts. A thoracotomy drainage was performed on June 24, 1947, followed by a 180 day course of streptomycin in preparation for further surgery. During this time the patient's temperature gradually dropped from an average of 103° to about 100° F. Streptomycin was continued throughout and for seventeen days after the Schede thoracoplasty to a total of 379 gm. Since the com-

pletion of the procedures the patient has remained completely afebrile and has only a small draining sinus at the site of his empyema two months postoperatively.

Two other patients, E. F. and H. H., are considered to have been afforded considerable protection by the streptomycin throughout their operations in view of the contralateral disease present in both patients. A preoperative course of 114 days of streptomycin in E. F. (No. 8) assisted a pneumothorax in controlling the active disease in the contralateral lung. A three stage, seven rib thoracoplasty was completed without any complications and the contralateral pneumothorax maintained throughout.

The other poor risk patient, H. H. (No. 13), appeared toxic with an unstable contralateral disease preoperatively but withstood a three stage, seven rib thoracoplasty assisted by 88 gm. of streptomycin given 1 gm. a day for twelve days preoperatively and thirty-seven days postoperatively as well as between stages. His sputum has remained negative for the twelve months that have elapsed since second stage thoracoplasty.

One patient, A. H. (No. 9), with bilateral disease did not respond favorably to streptomycin despite a preoperative course of 131 days and a total dose of 280 gm. The streptomycin was discontinued ten days after the beginning of the thoracoplasty on account of progressive tinnitus and deafness, so this patient did not get the full benefit of the drug throughout his operative procedures. An eight rib thoracoplasty was completed in three stages but the patient continues to have an intermittently positive sputum six months postoperatively.

A total of eleven patients have had the benefit of streptomycin preceding and during their thoracoplasties, ten of which have had completely satisfactory results. The two cases presented above in detail, Nos. 1 and 7, are considered to represent phenomenal responses to streptomycin, without which they would never have become acceptable for surgery.

The next two patients, Nos. 8 and 13, are considered to have remarkably fine results, a large part of the credit for which should be attributed to streptomycin in view of their bilateral disease. The remaining six patients who received streptomycin for their thoracoplasties probably could have achieved the same result without it.

In contradistinction to the streptomycin-treated thoracoplasties is a series of ten controls without streptomycin before or during their operations. In this group of ten patients three required streptomycin postoperatively to assist in controlling their disease and converting their sputum. In one of these patients, G. B. (No. 18), a contralateral pneumothorax was lost during the thoracoplasty and the streptomycin was started seven months postoperatively. This was continued for four and

Fig. 462



Fig. 463



Fig. 464

Fig. 465

Fig. 462 (F. W., No. 29).—Organized mixed tuberculous empyema collapsing left lung.

Fig. 463 (No. 29).—Complete reexpansion of lung thirteen days following decortication of mixed tuberculous empyema.

Fig. 464 (No. 29).—Lipiodol demonstrating residual left basilar empyema cavity.

Fig. 465 (No. 29).—Posterior-anterior chest x-ray at time of discharge; empyema and sinus completely healed. Patient clinically well.

one half months, although the sputum was converted within one month. Another patient, L. Y. (No. 19), developed a contralateral spread following a revision of a previously unsatisfactory thoracoplasty performed

## ANALYSIS OF TWENTY-NINE CASES

Patient No	Initials	Age	Lesion	Preoperative Duration	Operations		Streptomycin (gm.)			Results, Sputum		Comment and Follow up
					Stage	Ribs	Total Days	Total Dose	Preop	Conversion		
THORACOPLASTIES												
1	L D	22	1 Pul TB, LUL, F.A. 2 Mixed TB empy-ema, lt 3 Mult TB sinuses, lt	24 mos	4	8 (Schubel)	259	470	288	Neg	Neg prior to streptomycin	Excellent results Gaining wt Well 3 mos P O
2	J R	30	M F.A., LUL, with cavitation TB empy-ema, lt	39 mos	2	Thora- coplasty resection	102	113	57	Neg	Pos prior to 10 days streptomycin and neg at all times thereafter	Excellent results Well 4 mos P O
3	M L	27	M F.A., RUL, with cavitation	13 mos	2	7	63	63	32	Pos	34 days, immediately neg following 2nd stage	Excellent results Well 4 mos P O
4	L J	26	M F.A., RUL and RML	39 mos	2	9	116	116	61	Neg	Neg at last post prior to streptomycin	Excellent results 2 mos P O
5	W S	28	M F.A., LUL, with cavitation	9 mos	2	5	91	91	20	Pos	53 days (neg at 3rd stage)	Excellent results Left against advice 4 mos P O
6	W K	39	M F.A., bilat with cavitation, left	12 mos	2	6	67	47	14	Neg	Neg at bed rest prior to streptomycin	Excellent results Symptom-free, afebrile, 4 mos P O
7	R P	26	1 P A., LUL, with cavitation 2 TB empy-ema, lt 3 TB laryngitis 4 Contralateral spread, RUL, slight	11 mos	5	11	462	213	153	Neg	27 days	Excellent results Asymptomatic 5 1/2 mos P O

No.	Sex	Age	Weight	Height	Temp.	Pulse	Respiration	Condition	Remarks
1	♂	10	10.5	10.5	100	100	100	100	Excellent results. Maintained anastomosis.
2	♀	10	10.5	10.5	100	100	100	100	Strepto ulcers 1d because of tinnitus and deafness. Sputum intermittently pos. No wt gain. Fair condition 7 mos. P.O. Prognosis fair.
3	♂	10	10.5	10.5	100	100	100	100	Contractal spread P.O. to L.L. Cilia good. Sputum neg.
4	♀	10	10.5	10.5	100	100	100	100	Sputum neg. Cilia excellent 8 mos. P.O.
5	♂	10	10.5	10.5	100	100	100	100	Sputum neg. Cilia, excellent 10 mos. P.O.
6	♀	10	10.5	10.5	100	100	100	100	Sputum neg. Cilia excellent 11 mos. P.O.
7	♂	10	10.5	10.5	100	100	100	100	Sputum neg. Cilia excellent 11 1/2 mos. P.O.
8	♀	10	10.5	10.5	100	100	100	100	Sputum pos. Left against advice 11 mos. P.O.
9	♂	10	10.5	10.5	100	100	100	100	Died from transfusion reaction P.O. 3rd stage.
10	♀	10	10.5	10.5	100	100	100	100	Sputum pos. Left against advice 11 mos. P.O.
11	♂	10	10.5	10.5	100	100	100	100	Sputum neg. Strepto, started 7 1/2 mos. P.O. Cilia, fair to good; it cav. healing.
12	♀	10	10.5	10.5	100	100	100	100	Sputum pos. Left against advice 2 mos. P.O.; developed contractal spread. Cleared in 3 wks.



## ANALYSIS OF TWENTY-NINE CASES—Continued

Patient No	Initials	Age	Lesion	Preoperative Duration	Operative			Streptomycin (gm.)			Results Sputum		Comment and Follow-up
					Stages	Ribs		Total Days	Total Dose	Total Preop	Preop	Conversion	
20	L. S.	22	F. A., RUL, with rt TB empyema	24 mos	4	II		0	0	0	Neg	Occured preop	Sputum neg Clin excellent 1 1/2 mos P.O. 4th stage
21	R. L.	24	P. A., LUL, with lt TB empyema	18 mos	2	E		0	0	0	Pos	No conversion	Died from hemorrhage 2nd stage
LOBECTOMIES													
22	M. W.	25	Tuberculosis, LLL	19 mos	Lobectomy S			25	45.0	15.0	Neg	Never pos	Well despite leaving against advice 2 1/2 mos P.O.
23	C. A.	21	M. F. A., bilat with cav LLL (H <sup>+</sup> )	28 mos	LL Lobectomy			128	128	70	Neg	20 days	Excellent results Well 4 1/2 mos P.O.
24	O. C.	22	F. A., RLL, with cav	15 mos	Lobectomy C			0	0	0	Pos	Immediate P.O.	Well despite leaving 2 mos P.O. against advice
25	G. S.	24	Tuberculosis, LLL	16 mos	Lobectomy S			0	0	0	Neg	Never pos	Well
26	C. K.	22	F. A., RLL, with cav	7 mos	Lobectomy C			120	120	0*	Pos	510 days P.O. with and of strepto	Developed spread to lt lung P.O. with particular cavity Progress guarded
27	R. B.	20	Fibrous pneumonia, RLL, with bronchiectasis	23 mos	Lobectomy C			0	0	0	Neg	No pos	Well
28	M. B.	20	F. A., LUL, and bronchiectasis LLL and ling	37 mos	Lobectomy C Lung			0	0	0	Pos	Transitory 9 mos	Sputum pos 1 1/2 years later was a deeper site risk, having had 100% 4 stage thoracoplasty

## DECORTICATION and THORACOTOMY REVISION

29	F W	22	Mixed staph aureus and TB empyema	3 1/2 mos		D T	1 0	0 105	0 110	0 0	Neg Sinus pos	Never pos 6 mos for sinus to heal	Well	Sinus and empyema healed.
				5 mos										

F A, M F A, M A = Far advanced, moderately far advanced, moderately advanced

\* Control patient requiring streptomycin postoperative

## ANALYSIS OF TWENTY-NINE CASES—Concluded

Patient No	Initials	Age	Lesion	Preoperative Duration	Operations		Streptomycin (gm.)			Results Sputum		Comment and Follow-up
					Stages	Rebs	Total Days	Total Dose	Total Prep	Preop	Conversion	
20	L S	22	F A, RUL, with rt TB empyema	24 mos	4	11	0	0	0	Neg	Occurred preop	Sputum neg Clin excellent 1st mos P O 4th stage
21	R L	24	F A, LUL, with lt TB empyema	18 mos	2	5	0	0	0	Pos	No conversion	Died from hemorrhage 2nd stage
LOBECTOMIES												
22	M W	20	Tuberculosis, LLL	15 mos	Lobectomy S	1	25	45.0	18.0	Neg	Never pos	Well despite leaving against advice 3d mos P O
23	C A	21	M F A, biat with cav LLL (4*)	28 mos	LL lobectomy	1	123	129	79	Neg	29 days	Excellent results Well 4d mos P O
24	G C	22	F A, RLL, with cav	15 mos	Lobectomy C	1	0	0	0	Pos	Immediate P O	Well despite leaving 2 mos P O against advice
25	G S	34	Tuberculosis, LLL	16 mos	Lobectomy S	1	0	0	0	Neg	Never pos	Well
26	C K	32	F A, RLL, with cav	7 mos	Lobectomy C	1	129	120	0*	Pos	310 days P O with aid of strepto	Developed spread to lt lung P O with paravilar cavity Prognosis guarded
27	R B	20	Fibrocavous pneumonia, RLL, with bronchiectasis	23 mos	Lobectomy C	1	0	0	0	Neg	No pos	Well
28	M B	36	F A, LUL, and bronchiectasis, LLL and ling	33 mos	Lobectomy C Lung	1	0	0	0	Pos	Temporary 9 mos	Sput pos Prog poor Pt was a desperate risk, having had prev 4 stage thoracoplasty

who had not received streptomycin preceding or during their operations all cleared eventually on streptomycin but should not have occurred if the drug had been available preoperatively. In ten control thoracoplasty patients there were three spreads, reactivations of disease or failures to convert the sputum, whereas only one failure of sputum conversion occurred in those patients who were prepared preoperatively with streptomycin despite the poor risk patients included in this latter group.

A sufficiently long preoperative course of streptomycin to stabilize the disease, reduce or convert the sputum, reduce the fever and clear any active disease in the contralateral lung seems indicated, even though it may require a period of four or five months of constant treatment.

No toxic effects on the eighth cranial nerve were noted in any patients who received only 1 gm. of streptomycin a day, according to the revised protocol, in contrast with two such complications when the 2 gm. a day dosage was used.

### CONCLUSIONS

1. Preoperative preparation of tuberculous patients with streptomycin seems to offer distinct advantages.

2. Acutely ill and otherwise unstable patients can be converted into suitable surgical candidates as exemplified by the six patients described in this report.

3. A sufficiently long preoperative course should be provided to stabilize the disease, reduce or convert the sputum, reduce the fever and clear any active disease in the contralateral lung.

4. A reduction of the dose of streptomycin to 1 gm. a day seems to have greatly reduced its toxicity and eighth cranial nerve injuries.



## DECORTICATION OF THE UNEXPANDED TUBERCULOUS LUNG FOLLOWING INDUCED PNEUMOTHORAX

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THE revival of interest in the procedure of pleural decortication marks one of the great advances in thoracic surgery. The extension of its use into the realm of tuberculous empyema has led to its use in the therapy of a not infrequent and difficult problem: that of unexpanded lung following pneumothorax therapy for intrapulmonary tuberculosis. The end result has been the preservation of the lung and the removal of the mediastinal structures and contracture of the thoracic cage. There is the further possibility of development of tuberculous empyema, a condition which has heretofore been characterized by high morbidity and mortality, and has at best required mutilating surgical procedures to effect its obliteration.

Somner and Mills in 1946 described the accidental performance of decortication of a tuberculous pleuritis which went on to satisfactory healing. At the meeting of the American Association for Thoracic Surgery of what is, so far as we know, the first planned operation of decortication for the treatment of unexpanded tuberculous lung followed induced pneumothorax.

### PATHOLOGY

The pathologic changes seen with tuberculous pleuritis following pneumothorax are of more than academic interest. The principal alterations seen are:

1. Contraction of the lung leaving a pleural space which is potentially an empyema cavity.
2. Attempt at obliteration of the pleural space with shifting of the mediastinum.

The dangers of the former are obvious and are generally recognized. The

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latter changes, while understandable and recognized, are too frequently considered to be inconsequential. The shifting of the mediastinal structures to the affected side creates circulatory embarrassment of greater or lesser degree.

- 3 Thickening of the parietal layer which tends to restrict the complementary excursion of the thoracic cage, and thus create a handicap to respiration.

The gross changes in the five cases included in this report have been variable. In some a shaggy membrane was seen with a distinct plane of cleavage between the tuberculous membrane and the true pleural membrane. In others the membrane was intimately adherent to the visceral pleura. One case presented both types of reaction. On the average, the parietal pleural membrane was three times thicker than the visceral. A constant finding has been the flattening of the lung against the mediastinum, leaving the hilar and most of the mediastinal portions of the lung uninvolved. The greatest thickening of the membranes of both parietal and visceral surfaces was at the apex. In portions of the lung with underlying disease, the visceral membrane was firmly adherent to the lung, and in some cases it was impossible to find a plane of cleavage. Occasionally, there was symphysis between the parietal and visceral membranes. In two cases, folding of a portion of the lung was discovered. One of these showed folding of the lingula onto the upper lobe with resulting atelectasis.

It was usually impossible to determine the degree of the infectious process from the gross appearance of the visceral and parietal layers. However, microscopic examination of sections in all cases revealed areas of caseation necrosis and typical epithelioid tubercles with Langhans type giant cells in both the visceral and parietal membranes.

#### INDICATIONS FOR SURGERY

We have considered two indications for decortication of the unexpanded lung following induced pneumothorax (Table 1).

- 1 No change in the unexpanded lung is seen over a period of months. In all of our cases it was noted that fluid development had occurred and was persistent, that the presence of a membrane appearing both over the lung structure and the parietal pleura was noted comparatively early after fluid development. In one case the thickening over the lung structure was noted two months prior to the development of fluid. After pneumothorax had been abandoned, the lung appeared to expand to a certain level, where it remained without changing its volume.

2. In one case, which we feel is representative of an extremely important indication for decortication, the lung continued to expand after

TABLE 1

INDICATIONS FOR DECORTICATION OF THE UNEXPANDED LUNG AFTER INDUCED PNEUMOTHORAX IN THE FIVE CASES TO BE REPORTED

Duration of Pneumo-thorax Before Abandoning	Fluid Development after Start of Pneumo-thorax	Fluid Persistence	Unexpanded Lung Showing No Change	Time Development of Thickened Membrane after Start of Pneumo-thorax	Observation of Pleural Thickening	Displacement of Mediastinal Structures	Thorax Changes	Inspiratory Expiratory Films	Fluid Cultures
1. 10 mos	8 mos	Constant	4 mos.	6 mos	No change	Shift—6 mos	Narrow I.S.	Complete fixation	Negative
2. 7 mos	7 mos	Constant	6 mos	7 mos	Increasing	Shift—8 mos	Narrow I.S.	Partial fixation	Positive G.P.
3. 1½ mos	2 mos	Constant	5 mos.	5 mos	No change	Shift—7 mos	Narrow I.S.	Partial fixation	Negative
4. 7 mos.	3 mos.	Constant	7 mos	1 mos.	Increasing	Shift—3 mos.	Narrow I.S.	Complete fixation	Positive
5. 4 mos	2 mos.	Constant	Expanding	3 mos	No change	Shift—1 mos.	Narrow I.S.	Shift to pneumo-thorax side	Negative



abandoning pneumothorax. With this expansion there was an increase of the shift of the mediastinal structures to the pneumothorax side. We have seen instances in which, after a period of years, the heart is rotated and pulled upward, the diaphragm is raised and fixed, and the opposite lung has become emphysematous to fill the mediastinal space. The patient's vital capacity by this time has decreased until even slight exertion produces dyspnea, and in addition, the patient has all the signs and symptoms of cor pulmonale.

### TECHNIC OF OPERATION

Each patient received 1 gm. of streptomycin daily in divided doses intramuscularly, beginning two weeks prior to surgery, and continuing for thirty-three to sixty-one days postoperatively, with one exception (Case IV). This patient received streptomycin intramuscularly plus 0.2 gm. thrice weekly intrapleurally for eighty-six days prior to surgery.

Fifty thousand units of penicillin were given intramuscularly every three hours for two days prior to operation, and for two weeks postoperatively; and at the time of surgery 1 gm. of streptomycin and 200,000 units of penicillin dissolved in a small amount of saline solution were instilled into the pleural cavity.

Anesthesia consists of a mixture of nitrous oxide, oxygen and ether, given endotracheally, supplemented with pentothal sodium intravenously. The patient is placed with the operative side uppermost, and incision is preferably made in the fifth intercostal space. It is not necessary to resect or divide a rib. The length of the incision is determined by the location of the area to be decorticated. It usually extends from the midscapular line posteriorly to the sternum anteriorly. After the pleural space is entered, the incised parietal pleural membrane is separated for a distance of several centimeters on each side of the incision to permit placement of the rib spreader. Once the pleural cavity is entered, the lung is inflated at least every twenty minutes. The separation of the parietal membrane is continued until the visceral reflection is reached. A plane of cleavage is then developed on the pulmonary surface, and the visceral membrane is separated by gauze and finger dissection. Occasionally it is necessary to divide fibrous synechiae by sharp dissection. The apex of the upper lobe is not decorticated if there is great resistance to blunt dissection. If depleuralization occurs, small areas are sewn over with interrupted No. 60 cotton sutures. Larger areas are repaired by covering the denuded areas with "fibrin foam."

By the time the decortication is completed, the lung will have been inflated several times and may have expanded sufficiently to fill the pleu-

ral cavity. French mushroom type catheters, No. 26, are placed in the second or third interspace anteriorly and in the sixth or seventh interspace posterolaterally. The thoracic wall incision is closed tightly in layers with interrupted No. 40 cotton sutures for the pleura and intercostal muscles, and No. 20 cotton for the extracostal muscles. Continuous cotton suture is used for the skin. The catheters are immediately attached to suction pumps, and 10 cm. of water-negative pressure is maintained until there is no longer escape of air or pleural fluid, usually a matter of five to seven days. Blood is given during and following operation as indicated.

### COMMENTS

Experience with five cases shows that decortication of the unexpanded lung can be accomplished with safety insofar as the immediate postoperative course is concerned. Thus it is possible in the cases of unexpanded lung to avert the tragic consequences of tuberculous empyema. The results seem to be the same whether decortication is performed within a month or two or after a period of a year or more. In this group the pathology has ranged from a moderately thickened, smooth membrane with a clear transudate of low specific gravity to a fibrinofibrous membrane, grossly encased, with suppurative fluid of high specific gravity.

The time of operation to avert shifting of the mediastinal structures is, on the other hand, an important consideration. The one patient (Case V) with displacement of the upper mediastinal structures toward the affected side shows no return of the structures to the normal position following decortication one month after operation, although the lung fills the pleural space. While this case may not be typical, it does indicate that decortication should be performed before marked shifting of the mediastinum takes place, if the crippling effects of disturbed circulation and respiration are to be avoided.

In one case (Case II) it was necessary to reopen the operative wound ten days after operation to seal several air leaks and to remove blood clots which interfered with pulmonary expansion. After the second procedure, the lung expanded fully. The difficulty of air leakage was avoided in the later cases by sealing the depleuralized areas with "fibrin foam."

In those cases in which the lung cannot be expanded completely, and where there is no reason to suspect accumulation of air or blood within the pleural cavity, one should perform early thoracoplasty (Case IV). The one case in which this was necessary was satisfactorily treated with partial removal of the first four ribs.

One of the remarkable features of the operation is the smooth post-

operative convalescence. There has been no sustained rise in temperature following operation, and healing of the incisional wound of the thoracic wall has been primary in all cases.

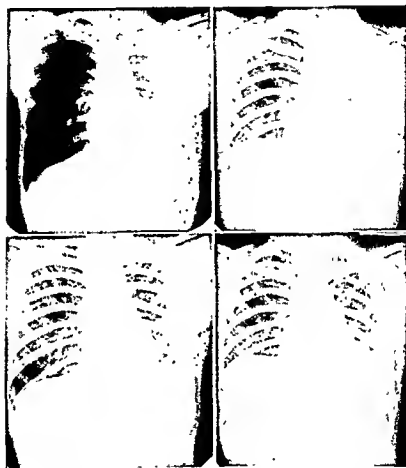


Fig 466 —Upper figures are inspiratory and expiratory films taken several days before decortication. Lower figures are inspiratory and expiratory taken three months after decortication.

### CASE REPORTS

**CASE I**—J. A. (Fig 466), aged 25, entered Birmingham Hospital April 16, 1946. Sputum was positive for *Mycobacterium tuberculosis*, and x-rays showed patchy infiltration and cavitation of the subclavicular region of the left lung. Therapeutic left pneumothorax was begun October 1, 1946. The sputum became converted, and the patient gained 30 pounds in weight. The patient left the

hospital, and returned to work against medical advice. He received pneumothorax refills as an outpatient between January and June 1947. He reentered the hospital June 12, 1947, with an effusion. Thoracentesis showed thin, greenish-yellow, clear fluid which was negative for acid fast bacilli on smear and culture. Pneumothorax was discontinued August 12, and a left temporary phrenic paralysis was performed August 15, 1947. The lung failed to expand following discontinuance of pneumothorax, and decortication was decided upon.

The patient was placed on streptomycin therapy November 10, 1947. Operation of decortication was performed November 24, 1947. An intercostal incision was made. The parietal pleural membrane was 7 mm. in thickness, and the visceral pleural membrane varied between 3 and 4 mm. in thickness. The membrane was rough and contained discrete areas of green inspissated fibrinopurulent material. The parietal membrane was removed except for a small area over the apex, at which point it was fused with the visceral membrane. The visceral membrane was removed with relative ease, except for several small areas which required sharp dissection. Smears and cultures of the fluid removed at the time of surgery showed *Mycob. tuberculosis*.

The postoperative course was uncomplicated. Expansion of the lung was complete on the second postoperative day, and the catheter was removed on the fifth postoperative day. X-ray examination five months after the operation showed complete lung expansion and no appreciable pleural thickening.

**CASE II.**—J. E. (Fig. 467), aged 23, entered Birmingham Hospital on August 2, 1949. Sputum was positive and x-ray revealed a dense exudative infiltration in the right upper lobe with multiple small cavities. Right therapeutic pneumothorax was started in September. An intrapleural pneumolysis was performed in November 1949. The patient left the hospital against medical advice in February 1947, and was readmitted April 25, 1947, with pleural effusion. Pneumothorax was abandoned at that time. Pleural fluid was positive for *Mycobacterium tuberculosis* by guinea pig inoculation on August 6, 1947.

The patient was placed on streptomycin November 17, 1947. The operation of decortication was performed on December 1, 1947. An intercostal incision was made. The parietal pleural membrane was found to be 1 cm. thick on the thoracic wall and 0.5 cm. thick over the diaphragm. The visceral pleural membrane measured 0.6 cm. in thickness. The parietal and visceral membranes were adherent in several areas with loculations containing seropurulent greenish fluid. The membranous surfaces were shaggy and showed areas of greenish thickened fibrinous exudate. The parietal membrane was removed. The visceral membrane was separated with great difficulty and in doing so, the pleura was penetrated in several areas. These areas were repaired with interrupted cotton sutures. The specific gravity of the fluid removed at surgery was 1.030 with one-third sediment on standing. Culture of the fluid was positive for *Mycob. tuberculosis*. Only one intrapleural catheter drain was used and suction was delayed for six hours in this case.

Consecutive x-rays up to the ninth postoperative day revealed the presence

of air and fluid in the pleural space. Consequently, the previous operative wound was reopened, and large amounts of clotted blood were removed from the pleural cavity. An organizing blood clot was peeled from the lung and three lacerations in the pleural surface were closed by suturing "fibrin foam" over the openings. Two intrapleural catheter drains were used on this occasion. The postoperative

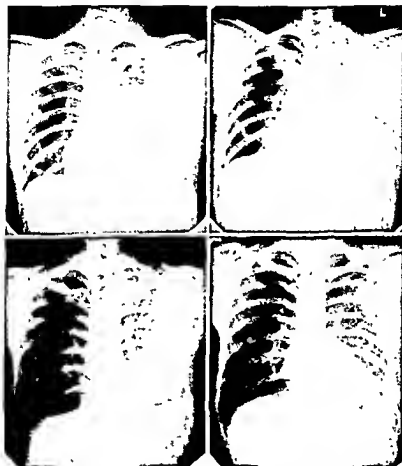


Fig 467 — Upper figures are of inspiratory and expiratory films taken several days before decortication. Corresponding lower figures are of films taken two months after decortication.

course was uneventful. Examination four months after operation showed complete lung expansion and mild pleural reaction.

CASE III — H. K., aged 23, was admitted to Birmingham Hospital April 26, 1946. Sputum was positive, and x-rays showed soft infiltrative disease in the upper two thirds of the left lung with cavitation at the second interspace. Left

therapeutic pneumothorax was begun in May 1946. Fluid developed two months after initiation of the pneumothorax, but it was not abandoned until June 1947. A left temporary phrenic paralysis was done June 1947. Repeated aspirations were unsuccessful in reexpanding the left lung.

The patient was placed on streptomycin January 15, 1948, and decortication was performed on January 28, 1948 through an intercostal incision. The parietal membrane measured 1 to 1.5 cm. in thickness. The visceral membrane measured 0.2 to 0.4 cm. in thickness. The surfaces were relatively smooth. The parietal membrane was removed with ease and the separation was continued onto the visceral surface, removing the entire membrane in one piece.

The postoperative course was uneventful. One catheter was removed on the seventh and the other on the ninth postoperative day. X-ray examination two months after the operation showed complete expansion of the lung and mild pleural reaction.

CASE IV—W. S., aged 26, was admitted to Birmingham Hospital March 6, 1947. A right therapeutic pneumothorax was begun elsewhere in February 1946, followed by pneumonolysis and spontaneous pneumothorax, in two and three months, respectively. Fluid developed at this time. When he entered this hospital, the pleural fluid was purulent and present in large quantity. Smears and cultures of the fluid were positive for *Mycobacterium tuberculosis*.

The patient was placed on streptomycin, 1 gm. daily intramuscularly in divided doses and 0.2 gm. thrice weekly intrapleurally, right, beginning November 5, 1947. Decortication was performed January 30, 1948 through an intercostal incision. The parietal membrane was 5 to 8 mm. in thickness and was intimately adherent to the thoracic cage. The visceral membrane varied in thickness from 3 to 5 mm. and was intimately adherent to the lung. There was complete symphysis between visceral and parietal membranes at the apex of the upper lobe, and over the anterior portion of the lower lobe. During the procedure of decortication, a caseous abscess about 1.5 cm. in diameter was entered and 3 cc. of whitish yellow caseous material exuded into the pleural space. This opening, as well as several depleuralized surfaces on the lung, was closed with interrupted cotton sutures. An area of bleeding at the apex of the thoracic cage was satisfactorily controlled with oxyeel gauze. After decortication, the lung could be expanded by positive pressure to only about three-fourths of its normal volume.

The patient's general condition was very satisfactory following operation, although the upper lobe failed to expand completely. This had been anticipated due to the great amount of disease in this portion of the lung. A thoracoplasty with removal of the first four ribs, and transverse processes of the second, third and fourth dorsal vertebrae was performed April 1, 1948. The space between the contracted upper lobe and the thoracic cage was closed. The patient's condition has been satisfactory up to the time of writing.

CASE V.—E. B., aged 26, was admitted to Birmingham Hospital March 6, 1947. Sputum was positive for *Mycobacterium tuberculosis*.

tion showed a multilocular cavity in the upper left lung field. Therapeutic left pneumothorax was begun on August 5, 1947. Fluid developed late in October 1947, and the pneumothorax was discontinued December 1947. There was gradual expansion of the lung with concurrent shift of the mediastinum and progressive rise and fixation on the left diaphragm. A marked decrease in the vital capacity was also noted.

Streptomycin was begun March 3, 1948, and decortication was performed March 19, 1948. An intercostal incision was made. The parietal membrane was 3 to 6 mm in thickness, and the visceral membrane was approximately 1 to 3 mm in thickness. Both surfaces were moderately roughened. There were several loculations of clear amber-colored fluid between the two membranes. The parietal membrane was separated with relative ease. The visceral membrane was intimately adherent to the lung and was removed with difficulty, much of the separation being made by sharp dissection. Several depleuralized areas of parenchyma were repaired with cotton sutures.

X-ray examination on April 5 showed complete expansion of the lung with disappearance of all fluid and air, excepting a small accumulation of several cubic centimeters of air. There was no evidence of return of the mediastinal structures to the normal position. The postoperative course has been uneventful to the present time.

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## DECORTICATION IN TUBERCULOSIS\*

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SOME of the methods of treatment of tuberculosis require re-examination in the light of the development of new antibiotics in the control of the disease.

This report presents recent experience in the use of decortication in the treatment of the abnormal pleural space often associated with pulmonary tuberculosis. The existence of such spaces long has been recognized as a threat to health. Collapse therapy has been the generally accepted method of treatment but its shortcomings have been appreciated by all. Renewed interest in decortication followed the success with the method in handling the chest injuries of the recent war. The antibiotic action of streptomycin on the tubercle bacillus has justified further trial of decortication in these cases.

The risks of infection and other complications in a persistent pleural space have been and still are sufficient reasons for uniformly attempting its obliteration. Thoracoplasty as advanced by Estlander<sup>1</sup> in 1879 and modified by Schede<sup>2</sup> and others was designed to bring the chest wall to the collapsed and immobile lung. The hazard of the untreated condition has justified surgeons in accepting the well-known risks of such extensive procedures. In spite of many excellent results the frequent sacrifice of undiseased and functional lung has been appreciated as a disadvantage of the method. This evil is generally accepted only with reluctance and a definite rate of failure stimulated other approach.

Decortication for chronic empyema was described by Fowler<sup>3</sup> in 1893, and Delorme<sup>4</sup> in 1894, and is commonly known by the latter's name. It entails removal of the organized membrane from the immobilized and collapsed lung to permit its re-expansion. The modifications of Roux, Ransohoff, Lilienthal<sup>5</sup> and others have adhered to the same principle. Some excellent results followed decortication but after many failures it fell into disuse. It was often a prolonged and shocking operation. Post-operative hemorrhage and infection precipitated many recurrent empyemas, quite often more severe than the original. Expansion early after operation was frequently lost due to wound breakdown from infection.

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Re-expansion did not always follow successful decortication because of underlying defects such as parenchymal fibrosis, fistulas, or other active disease. Failure to recognize or control these factors led to unsatisfactory results.

During the recent war<sup>4, 7</sup> decortication was revived in the treatment of organizing hemothorax and pyogenic empyema with and without underlying pulmonary abnormality. The fairly uniform success attained by many operators is understandable. The previously healthy young soldier became an excellent surgical risk as a wounded patient, especially after adequate early care and preoperative preparation. The improvement in anesthesia and operative techniques permitted with safety the concomitant removal of injured lung by careful segmental or lobar resection. Chemotherapeutic agents, principally penicillin, contributed significantly by inhibiting the growth of organisms and postoperative infection. The incidence of recurrent empyema fell sharply. The ability to maintain a closed chest permitted adhesions between the pleural layers and prevented recollapse of the lung after successful re-expansion. Since streptomycin has resembled penicillin in inhibiting the offending organisms decortication has been successful in the treatment of a number of cases in which tuberculosis has been the dominant factor.

In applying decortication to tuberculosis two aims have commanded major consideration. The primary surgical intent has been closure of the pleural space. However, an equally important objective has been the desirability of maximal preservation of pulmonary function. Yet, in spite of these aims it is evident, as Gurd,<sup>8</sup> Eggers<sup>9</sup> and others have stated, that the status of underlying disease must govern the use of the procedure.

in certain selected cases. The unexpandable lung in which long pneumothorax has successfully arrested minimal disease has the most favorable outlook. Intrapleural infection often is minimal and being subject to control is only a small postoperative threat. Parenchymal changes are insufficient to prevent complete and early re-expansion. The membrane often is thin and easily removed. In several cases it has been peeled off rapidly without hemorrhage or shock and with excellent results. In tuberculous empyema with little systemic reaction the prospect is only a little

and maximal preservation of function of undiseased pulmonary tissue with surgery of minimal risk. When total re-expansion has been unsafe, plemented by thoracoplasty or by en used to minimize reactivation or has been completed for broncho- disease in combination with decortication. Its role is still not finally established but must await more experience.

Since one cannot disassociate the good effects of decortication from its possible ill effects without cautious regard for the status of the disease, the course of any tuberculous patient must be resurveyed in detail before decortication is attempted. It must be remembered that decortication obliterates the space by re-expansion of the lung. If such re-expansion may adversely affect the disease, simple decortication should not be applied. Occasionally it may be combined with collapse or excisional methods.

The technic of decortication in tuberculosis has not varied from that in other disease. The chest has been opened gradually with or without rib resection as the lung has been mobilized toward the mediastinum to avoid tearing. In some the membrane has peeled easily from the lung but in

age tubes secondary removal of large blood clots occasionally has been necessary. Meticulous attention to the details of surgical technic including adequate exposure, neat, gentle and visual dissection with lobar or complete mobilization of the lung including the fissures and chest wall and diaphragm have warranted the time spent. Postoperative care with particular attention to bronchial toilet and the intrapleural and intramuscular use of streptomycin have definitely enhanced the possibilities of the procedure.

### ILLUSTRATIVE CASES

The following case reports illustrate the extent to which the authors have employed decortication alone and in conjunction with other procedures.

CASE I (No. 97456\*).—A 20 year old colored naval veteran was admitted July 23, 1947, with tuberculosis of the left lower lobe with cavitation and (Fig 468) positive sputum but negative bronchoscopy. He was treated by bed rest.

On August 17 he developed a left hydropneumothorax with temperature of 105.6° F. (Fig. 469). Direct smear of the yellow cloudy aspirate showed tubercle bacilli but no pyogens on culture. On August 19, after the administration of

streptomycin and penicillin, underwater catheter drainage was instituted. Figure 470 shows the expansion obtained before the tube was removed on September 4 when he was afebrile.

Fig 468

Fig 469

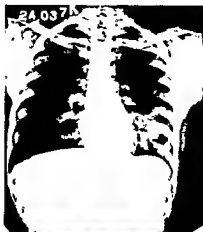


Fig 470

Fig 471

Fig 468 (Case I) — 8/8/47. Note parenchymal cavity and fluid level in the left lower lung field.

Fig 469 — 8/8/47. Note left hydropneumothorax.

Fig 470 — 8/20/47. Note reexpansion following catheter drainage under water and infiltration in right lower lung field.

Fig 471 — 11/24/47. Note extent of thickening of pleura 2 days before operation. Infiltration on right has cleared well.

Fluid, persistently positive only for tubercle bacilli, reaccumulated. Secondary closed suction drainage on September 22 was followed by clinical improvement.

but the lung failed to expand. A progressively thickening membrane with further lung collapse prompted the attempt to obtain closure by decortication since sputa and gastric examinations were now negative (Fig. 471).

On November 26, 1947, a gray shaggy membrane 4 mm. thick was easily removed from the entire chest wall and lung except over one small area in the lower lobe. No bronchopleural fistula was demonstrated. After the instillation of streptomycin and the insertion of two drainage tubes the lung was easily re-expanded and the chest closed in layers. The tubes were removed by the fourth postoperative day. He had a satisfactory recovery with a subsequent weight gain of 20 pounds, loss of clinical symptoms and repeatedly negative cultures and smears for tubercle bacilli (Fig. 472). Between August 19 and December 19 he received 110 gm. of streptomycin.



Fig. 472 —2/19/48 Postoperative result after 3 months. No parenchymal cavity could be identified.

*Comment.*—This patient had a fairly acute tuberculous empyema. With demonstrated ability of the lung to expand decortication was chosen in preference to Schede thoracoplasty which could always be used. In the light of subsequent experience, lobectomy or segmental resection might have been advisable for the parenchymal lesion and bronchopleural fistula. The long term result is open to conjecture.

**CASE II (No. 95786\*).**—This 48 year old white man was discharged from the Navy in August 1946 as arrested left apical tuberculous after hospitalization for one year. In September 1946 following recurrence with cavitation at the left apex (Fig. 473) he was treated by pneumothorax and pneumolysis in another hospital. Fluid persisted and he was admitted on May 26th, 1947 with an exten-

\* Veterans Hospital Case.

sive left hydropneumothorax. The sputum was persistently negative but culture of the aspirate was positive for tubercle bacilli. Bronchoscopy was negative. Attempted expansion by repeated tapping (Fig. 474) was unsuccessful and on

Fig. 473

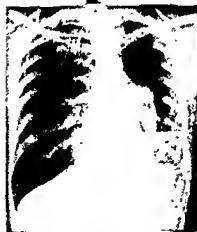


Fig. 474



Fig. 475

Fig. 473 (Case II) —9/19/46. Note extent of parenchymal disease in the left upper lung field.

Fig. 474 —9/13/47. Note extent of collapse and thickening of visceral pleura.

Fig. 475 —1/26/48. Postoperative result after 1 month. Fluid level at top is in the thoracoplasty space.

December 12, 1947, decortication was done. Because the upper lobe was the seat of extensive infiltration it was not decorticated. A thin membrane was easily stripped from the left lower lobe, chest wall and diaphragm. A four rib thoracoplasty was added. After the insertion of two tubes and streptomycin the lower

lobe was easily expanded to fill the reduced pleural space and the incision was closed in layers. The tubes were removed on the third day. He received 30 gm. of streptomycin between December 23, 1947 and January 23, 1948. He has made an excellent recovery (Fig. 475).

*Comment.*—This patient had moderately acute tuberculous empyema, with satisfactory collapse of the diseased upper lobe. Lobar decortication saved much functional pulmonary reserve and in conjunction with thoracoplasty provided for closure of the space and maintenance of the parenchymal collapse.

CASE III (No. 100160\*) —In this 33 year old white man a left apical cavity was found in January 1946. Sputum was positive and pneumothorax was instituted in February 1946. In December 1946 he was discharged from the Army as arrested. Ten months later, in October 1947, after the cavity reopened with positive sputum he was admitted (Fig. 476). The left pneumothorax was continued until November 1947 when fluid developed which showed tubercle bacilli on culture. With an unclosed cavity yielding a positive sputum and a persistent pneumothorax with thickening of the pleura noted on x-ray, operation was planned to attack both problems.

On January 21, 1948, decortication of the left lower lobe, chest wall and diaphragm was easily completed and the left upper lobe which was extensively involved was excised by individual ligation technic. After the insertion of 2 gm. of streptomycin in 10 gm. of plasma and two drainage tubes the chest was closed in layers. Expansion of the residual lung filled the chest, the wound healed by primary union and the patient made a fine recovery (Fig. 477). On February 16, 1948, an upper six rib thoracoplasty with an apicolysis was added (Fig. 478).

*Comment.*—This patient had an upper lobe excavation and an undis-eased lower lobe collapsed under a membrane caused by tuberculous empyema in a pneumothorax space. Decortication and lobectomy seemed to offer more than any other course and proved satisfactory.

CASE IV (F. M.†).—Tuberculosis of right apex with positive sputum was first discovered in this 32 year old Porto Rican man in July 1946. He had bed rest until November 1946 when a right pneumothorax was induced and followed by pneumolysis in January 1947. Fluid which immediately followed was tapped repeatedly. Six months before admission to the hospital on January 22, 1948, thick pus positive for tubercle bacilli was aspirated. His scanty sputum was repeatedly negative by all methods.

\* Veterans Hospital Case.

† From the Chest Surgical Service, Columbia University Division, Bellevue Hospital, New York.

extremely difficult but was completed from apex to base including the diaphragm.  
After the insertion of two tubes and 3 gm. of streptomycin the decorticated ex-

Fig 476



Fig 477

Fig 478

Fig 476 (Case III).—10/1/47 Note left pneumothorax and open cavity in the upper lung field

Fig 477 —2/14/48 Result 8 weeks following right upper lobe lobectomy and decortication. There is a minimal pneumothorax space at the apex

Fig 478 —3/9/48 One month following thoracoplasty and apicolysis

panded lobes shifted the upper lobe and completely filled the space and the chest was closed in layers.

and the wound reclosed in layers. The patient made an uneventful postoperative recovery, the tubes being removed on the fifth postoperative day. He received streptomycin for thirty-five days

*Comment.*—This patient had minimal apical tuberculosis and tuberculous empyema. Collapse of the lesion was effected but had sacrificed much good lung. Lobar decortication with thoracoplasty was chosen to

Fig. 479

Fig. 480

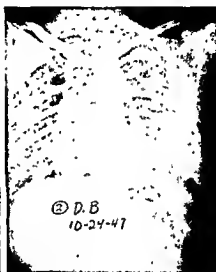
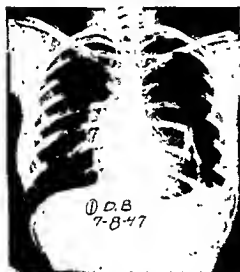


Fig. 479 (Case V) —7/8/47 showing unexpandable left lung. Cavity at right apex is shown better in the tomograph (Fig. 482)

Fig. 480 —Two days after left decortication

**CASE V (B. D.\*).**—This 30 year old white woman had onset of bilateral apical tuberculosis with a small cavity on the left in 1941. Since the cavity failed to close and the sputum remained positive on bed rest a left pneumothorax was induced in late 1941 and continued to 1946. The sputum converted soon after collapse was instituted and remained negative until 1946 when it again turned positive due to excavation at the right apex. Unsuccessful attempts to expand the left lung were followed by effusion (Fig. 479).

Decortication offered the possibility of regaining sufficient pulmonary function by expansion of the left lung to permit treatment of the right apical cavity. On October 22, 1947, a membrane 1 to 2 mm. in thickness was easily peeled from the entire left lung. After the insertion of two tubes and 1 gm. of streptomycin the lung readily expanded to fill the pleural space and the wound was closed in layers

\* From the Triboro Hospital, N. Y. C.



(Fig 480) The tubes were removed on the fourth postoperative day and the patient made an excellent recovery (Fig 481).

Fig 481

Fig 482



Fig 481—Twelve days after left decortication

Fig 482—Tomograph of right apical cavity



Fig 483—Result 117 days after left decortication and 75 days after right upper lobectomy

On December 2, 1947, a right upper lobectomy (Fig 482) was completed. The patient made another uneventful recovery. The sputum became negative and

finally disappeared, the cough ceased and the patient gained to her normal weight. She received 100 gm of streptomycin during her preoperative and post-operative period (Fig. 483).

*Comment.*—When this patient was admitted she had a markedly collapsed and unexpandable left lung with a right apical cavity requiring treatment. Without the ability to expand her left lung by decortication her outlook was almost hopeless. To decortication alone can be attributed the improvement in her future prospects.

### SUMMARY AND CONCLUSIONS

1. Experience with decortication in pulmonary tuberculosis is presented.

2. The short case reports illustrate the use of decortication alone and in combination with other methods.

3. The procedure has allowed obliteration of the pleural space in cases formerly subjected to extensive collapse procedures. At the same time the function of the pulmonary parenchyma has been maximally preserved.

4. The ability of streptomycin to inhibit the tubercle bacillus has contributed greatly to the success of the procedure by reducing the incidence of recurrent empyema and infected operative wounds.

5. The experience to date is extremely favorable and warrants further extensive use of the procedure. A complete follow-up of a large number of cases will be the only basis for proper evaluation of its effectiveness.

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# STREPTOMYCIN IN THE TREATMENT OF TUBERCULOUS ABSCESES AND SINUSES

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THROUGHOUT the past fifty years standard surgical textbooks have advocated conservative therapy in the treatment of tuberculous abscesses and draining sinuses. Christopher,<sup>1</sup> Calot,<sup>2</sup> Babcock,<sup>3</sup> Bancroft and Murray,<sup>4</sup> Steindler<sup>5</sup> and others have declared conservatism to be the keystone of treatment.

The substance of their opinions is contained in the statements by Bancroft and Murray<sup>4</sup> that tuberculous abscesses absorb or calcify and require no treatment. The strength of their conviction is apparent in the following warning: "It has been said that draining a tuberculous abscess frequently signs a patient's death warrant."

The discovery of the suppressive action of streptomycin against the *Mycobacterium tuberculosis* by Waksman<sup>6</sup> and others in 1944 has made possible a combination of surgical and antibiotic therapy of these lesions. This combined form of treatment has given results, in our hands, superior to those following either method used individually. During the past two years we have treated sixty-three patients who presented a total of 134 tuberculous abscesses or sinus tracts.

## TECHNIC OF TREATMENT

The primary principle followed in the treatment of these abscesses and sinuses has been the maintenance of adequate drainage of the lesion. When confronted with a tuberculous abscess we have not hesitated to make an ample incision, evacuate the necrotic debris and pus, and establish free drainage. This may be done before or during streptomycin therapy, but we believe that results are better if the operation is done after the patient has been on streptomycin for several days. The underlying bone lesion is excised when practicable. After the abscess has been incised and evacuated it is packed with gauze at the operating table. Several types of gauze have been used,—dry gauze, petrolatum or furacin-impregnated gauze. The packings are changed daily, and the outer dressings as needed. In all cases it is advisable to give streptomycin.

If a sinus tract is already present when the patient comes under our care, it is first debrided of as much of the necrotic tissue as possible. Then

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furacin or petrolatum gauze dressings are applied over the sinus tract to reduce secondary infection and to facilitate the removal of dressings.

Before streptomycin therapy was instituted the tuberculous etiology was established in each patient by biopsy of the tract or bacteriologic study of the drainage material. In the original series a daily dose of 1.8 gm. of streptomycin was arbitrarily established. In October, 1947, the dose was reduced to 1 gm. daily. This reduction was made in an effort to avoid the toxic manifestations and the development of resistance which had been encountered in the 1.8 gm. series. In a further effort to establish the minimal effective therapeutic dose a small group of patients were treated with 0.2 gm. daily.

The following case we believe indicates the importance of adequate drainage of a tuberculous abscess and the removal of the underlying cause.

**CASE I**—M. W., a 24 year old colored man, gave a history of an abscess in the left anterior chest wall of about a year's duration. This abscess pointed and ruptured, forming a small sinus tract. The abscess was found to be tuberculous and streptomycin was given, 1.8 gm. daily in divided doses of 0.3 gm. every four hours, and continued for ninety days. At the end of this time the sinus had ceased draining and the sinus opening was covered with a scab. Three weeks later a cold abscess developed in the same location in the chest wall and the sinus again started to drain. The abscess was incised and the third costal cartilage removed, a small area on the lateral surface of the sternum was also curetted. The area was then packed open with gauze. Dressings were changed daily after the third post-operative day. Streptomycin was given, using the same dosage as before and continued for sixty days. The large defect in the chest wall healed in six weeks and has remained healed for over a year and a half.

#### TUBERCULOUS SINUSES AND ABSCESSES ORIGINATING IN BONE OR JOINT

In this group there were thirty-one patients (Table 1) with 102 sinuses and abscesses originating in bone or joint lesions. The bones involved and the frequency of involvement are shown in table 2.

The duration of these sinuses was variable, the longest duration of a sinus before the institution of streptomycin was ten years. Many of the sinuses were created surgically before the course of therapy was begun, and some developed while the patient was being treated.

In most cases of tuberculosis of the spine a paravertebral abscess will develop at some time during the course of the disease process. The abscess will often spread by following connective tissue layers between muscles arising from the spine, or by following the layers of connective tissue around nerves and blood vessels after perforation of the anterior longitudinal ligament of the spine. One of the most common directions in which

this type of abscess is apt to spread is along the psoas muscle pointing in the groin. We have also noted paravertebral abscesses pointing on the posterior and lateral chest wall and in the lower lumbar region.

TABLE 1

TUBERCULOUS SINUSES AND ABSCESES ORIGINATING IN BONE OR JOINT

Daily Dosage Regimen	1 8 Grams	1 0 Grams	0 2 Grams	Totals
Number of patients	15	13	3	31
Sinuses	62	32	8	102
Sinuses healed	58	31	8	97
Sinuses improved	1	1	—	2
Sinuses worse	1	—	—	1
Sinuses unchanged	2	—	—	2

TABLE 2

SITES OF BONE AND JOINT LESIONS

	Number of Lesions
Spine .	14
Ribs	13
Sternum	3
Long bones of extremities . . .	4
Small bones of hands and feet	4
Clavicle	3
Ilium	2
Mandible	1
Skull (orbit)	2
Joints	10
Hip	1
Knee	2
Shoulder	2
Elbow	1
Sacroiliac	4
Total	56

In the case of a deep psoas abscess, it is difficult to secure adequate drainage, since the opening into the sinus tract tends to close too rapidly. To obviate this difficulty, we have opened the abscess and evacuated the pus, when the incision is partially closed a rubber catheter is introduced and the abscess irrigated daily along with instillation of penicillin and streptomycin into the abscess cavity. Streptomycin is also given intramuscularly. In this type of abscess particularly we feel that the combination of penicillin and streptomycin is valuable, for by the use of both

drugs we afford the patient protection against secondary invaders not affected by streptomycin. Bigger<sup>7</sup> in his work on the synergistic action of penicillin and the sulfonamides mentions the formation of penicillinase in the intestine during the parenteral administration of this drug. This substance then weakens the action of the parent drug. If this penicillinase is destroyed, however, the penicillin administered will retain its potency. Olsen<sup>8</sup> and Redewill<sup>9</sup> have advanced the theory that streptomycin and penicillin have a synergistic action. They pointed out the fact that when streptomycin is given orally large amounts accumulate in the intestine with the destruction of the penicillinase-producing bacteria, thus the action of the penicillin is enhanced by the use of streptomycin. We adopted the use of penicillin in combination with streptomycin early in the postoperative treatment of sinuses to reduce the number of secondary bacterial invaders.

Where it was impossible to remove the underlying bone or joint disease we have resorted to a conservative management of the lesion. Patients with spondylitis have been kept on a hard bed or placed in a body cast. In two cases after the paravertebral abscesses have been controlled spinal fusions have been performed with excellent results. In the cases with joint involvement with sinus and abscess formation we have attempted to immobilize the joint in the optimum position.

The two lesions about the orbit were unusual. Both patients had multiple areas of bone involvement with sinus and abscess formation. The orbital lesion in both produced a unilateral exophthalmos. These cases were included in the original group of cases treated with 1.8 gm. of streptomycin daily. In one case necrotic bone had been removed from the superior portion of the orbital plate eighteen months before streptomycin was started and a sinus had persisted. This sinus healed in ten weeks after streptomycin therapy was started and the exophthalmos receded. This patient received 150 days of streptomycin therapy.

The second patient had a lesion involving the lateral portion of the left orbital plate. This improved on 150 days of streptomycin. Four weeks after cessation of treatment the exophthalmos became more marked and a large abscess developed in the left temporal region. The patient was restarted on streptomycin and adequate drainage established and necrotic bone removed. The lesion then healed completely in eight months.

were never carried out.

We have not noted any definite changes in the bone lesions in this

series which could be definitely attributed to streptomycin alone. There has been improvement in most patients, but we can not be sure that rest and immobilization were not the most important factors. We do believe that streptomycin by its bacteriostatic action on the tubercle bacillus has stimulated the healing processes.

**Comment.**—In this series of cases we have had 95 per cent healing of the sinus tracts. In the majority, drainage decreases to a marked degree from the sixth to the tenth day, after which the sinus tract will begin to granulate in and close. With the 1.8 gm. or the 1.0 gm. dose, complete healing occurs in most instances in from two to twelve weeks, depending on the size and depth of the sinus tract. Where the dose of 0.2 gm. daily was employed healing occurred but was slower.

The failures in this group of patients were due to one of several factors; inadequate drainage, development of resistance, and inadequate streptomycin therapy. One patient died of a generalized spread of tuberculosis shortly after cessation of treatment. At autopsy a large abscess was found beneath the sternum that had been inadequately drained. This patient probably developed resistance to streptomycin as indicated by his downhill course but resistance studies were never carried out. Another patient with a deep lying abscess improved after drainage and treatment but failed to close. This failure was due to inadequate drainage. Two sinuses persist in another patient who developed a resistance to 1000 micrograms of streptomycin per cubic centimeter. The other failure was due to inadequate streptomycin therapy. This patient developed an exfoliative dermatitis after six weeks of treatment and discontinuation of the drug was mandatory.

#### SINUSES SECONDARY TO TUBERCULOUS LYMPHADENITIS

This series comprises four cases of tuberculous lymphadenitis with draining sinuses. All were cases of cervical lymphadenitis and the sinuses resulted after biopsy of these nodes. Duration of the sinuses prior to streptomycin therapy was from two and one-half to fifteen months. Table 3 shows the dosage, healing, and patients treated.

There was little change noted in the size of the lymph glands involved in any of the cases. In the one case in which the sinus failed to close, the glands increased in size and new ones appeared. A poststreptomycin biopsy was performed in one patient. Grossly the node presented the typical picture of a caseating lymph node and microscopically many tubercles were seen. The pathologic diagnosis was tuberculous lymphadenitis.

**Comment.**—This series is small but the results seem to suggest that streptomycin is of questionable value in the treatment of tuberculous



lymphadenitis The drug is definitely valuable in the closure of sinuses from these glands if the organism isolated is sensitive to streptomycin. We believe that with streptomycin, excision of these nodes when indicated can be carried out with the expectation of obtaining primary healing without sinus formation.

### GENITAL SINUSES AND ABSCESSSES

One of the most difficult problems encountered on the urological service of a tuberculosis sanatorium is the treatment of draining sinuses of the scrotum, both spontaneous and postoperative. Since the advent of streptomycin and its use under close observation, we have been able to evaluate results under varying dosage. Streptomycin has been given in accordance with the protocols established for the treatment of tuberculous sinus tracts and fistulas and also those separate protocols for tuber-

TABLE 3  
RESULTS IN SINUSES SECONDARY TO TUBERCULOUS LYMPHADENITIS

Dosage Regimen	1.8 Grams Daily	1.0 Grams Daily	0.2 Grams Daily
Number of patients	2	1	1
Sinuses	2	1	1
Sinuses healed	1	1	1
Sinus unchanged	1	0	0

culous infections of the pulmonary, endobronchial, renal and osseous systems.

These sinuses were divided into three groups as illustrated in Table 4. Duration prior to treatment ranged from four to thirteen months, with one exception, that of a patient with two sinuses of five years' duration. The group in Protocol I (2 gm.) consist of seven patients who displayed the greatest degree of vertigo. Here six of the seven experienced severe to moderate dizziness. The second group of patients in Protocol II (1 gm.) had less vertigo, only four of the seven complaining of moderate dizziness. In the third group in Protocol III (0.2 gm.), only one of the seven noted moderate vertigo. By comparison this third group would appear to have been on the dosage of choice as regards toxicity.

In comparing results on cessation of drainage and healing of the sinus tract, it was noted that the recovery period in the Protocol III (0.2 gm.) group was twice as long as in the other two. In this group, also, there is to be noted one failure with recurrence of drainage sixty days after completion of treatment. Subsequent surgery revealed that a small portion of the epididymis was still present, which accounted for the result ob-

TABLE 1  
GENITAL SINUSES AND ABSCESSSES

Protocol	No. of Patients	Average Duration Prior to Treatment	Duration of Treatment	Vertigo			Average Results		Failures
				S	M	0	Drainage Ceased	Healed	
Protocol I 2 gm. (0.4 gm. q. 4 hr. for 5 doses)	7	13 mos.	120 days	3	3	1	7 days	14 days	0
Protocol II 1 gm (0.5 gm b.i.d.) and 0.2 gm. q. 4 hr. for 5 doses	7	5 mos	120 days	0	4	3	9 days	15.5 days	0
Protocol III 0.2 gm. q d.	7	1 mos.	120 days	0	1	6	15 days	13 days	1*

S—Severe

M—Moderate

0—None

\* Recurrence 60 days after treatment was completed.

tained in this patient. Results in response to therapy were almost identical, with narrow margin, in Protocols I and II, since there was less vertigo in the second group, the latter would appear to be the preferable dosage.

A final factor which we must consider is the possible relationship between dosage and resistance. As we previously noted, the combined Veterans Administration experience indicates that the duration of treatment rather than dosage is responsible for increased resistance levels. Therefore, with this in mind, we can safely select the 1 gm. dosage with an average healing period of fourteen days rather than the 0.2 gm. dosage with an average healing period three times longer in duration.

The value of surgery in conjunction with streptomycin is again demonstrated in the observation of three patients referred to the genitourinary service in whom epididymitis and orchitis developed during the course of therapy of the antibiotic. In two patients with tuberculous meningitis and a third with *miliary pulmonary tuberculosis*, *scrotal swelling* appeared during the second and third months of streptomycin treatment. In all surgery was contraindicated, but they were continued on streptomycin. Two expired after four and five months, respectively, but the third was able to undergo an orchidectomy after six months. However, the streptomycin had to be discontinued in this instance because the patient developed severe vertigo. Prior to orchidectomy the testicular abscess ruptured and drained, leaving a sinus tract. Following operation the sinus opened again, and drainage has persisted to date.

Three additional cases gave us the opportunity to treat epididymitis with what we felt was the optimum of therapy. Streptomycin was given for from seven to nine days after the diagnosis was made. Surgery was then done and the patient received streptomycin for 120 days for coexisting disease. Postoperative primary healing resulted in all instances in seven days. Figure 484, *A* and *B* shows the appearance of the operative wound in two patients, both of which were photographed seven days after operation. In both of these patients the epididymal abscess ruptured during surgery. In *A* streptomycin therapy was begun seven days preoperatively, in *B* the patient underwent surgery without the benefit of streptomycin. The appearance in the latter patient on the tenth day of streptomycin therapy (0.2 gm. once every day) is shown in *C*. The latter patient healed on the fortieth day of treatment.

Comment.—Here again, in this genital series, the best results to date were obtained by removal of as much of the tuberculous abscess and tissue as possible by surgery in conjunction with streptomycin, 1 gm. daily given preoperatively. Streptomycin alone has been of definite value only in those cases in which adequate drainage is present and in which

the underlying pathology has been excised as in the postoperative sinus cases.

Pathologists are seeking evidence in autopsic and surgical material of the effects of streptomycin healing, on the assumption that streptomycin does aid in the healing process as well as affording antibiotic action. Genital tuberculosis has offered an excellent source of specimens; if therapy is successful in the other categories, no material is available for study on arrest of the disease process. In those cases in which the primary treatment is directed toward closure of the sinus tract, to be followed later with surgical removal of the lesion, and when orchitis and epididymitis occur during the course of treatment, many interesting specimens



Fig 484—Results in epididymitis seven days postoperatively with and without streptomycin therapy. In *A* streptomycin therapy was begun seven days preoperatively; in *B* no streptomycin was employed. The appearance of the latter patient on the tenth day of streptomycin therapy is shown in *C*.

have been obtained. Microscopic examination of these specimens has revealed early fibrosis, marked infiltration and accumulations of polymorphonuclear leukocytes, many of which are eosinophilic. In addition, Langhans giant cells are seen in abundance, containing many nuclei varying in size. This microscopic picture is at distinct variance with specimens from similar cases with the same duration of involvement in which surgical removal was done without previous streptomycin therapy. Here sections have failed to show specifically any eosinophilia or excessive giant cell formation. This is merely an observation, and more intensive study of other organs is needed for any worthwhile deductions. Huffines<sup>9</sup> in another series and Bornstein<sup>10</sup> have both noted the same microscopic changes.

## GENERAL CUTANEOUS SINUSES AND FISTULAS

Of absorbing clinical interest are a small group (Table 5) of sinus tracts which we have had the occasion to follow, along with the others in this series. In all seven patients the sinuses and fistulas developed following surgical procedures. In four of the seven patients no adjunctive surgical treatment was done and, in addition, two of this group failed to respond to therapy. Further description of these two patients is warranted. The patient who developed a dehiscence of his thoracoplasty wound resisted all attempts at excision, revision and immobilization for five years. And, although healing was incomplete at the end of 120 days we were unable to culture acid-fast bacilli from the area after the seventh day of therapy.

The second patient who failed to respond to treatment was prepared for pneumonectomy, receiving 1 gm. of streptomycin daily for one month preoperatively. Exploratory thoracotomy proved the procedure inoperable and a resultant sinus tract formed on the twenty-fifth postoperative day. As previously noted in Table 5, streptomycin was discontinued on the fortieth day without evidence of healing, although some decrease in drainage was noted.

The diagnosis of ureterocutaneous fistula in the first patient in the series (Table 5) was confirmed by lipiodal studies of the sinus tract, plus the excretion of renal function dye through the wound. In addition the wound had a characteristic odor of urine with copious amounts of thin, watery drainage which necessitated frequent changes in dressings. This ceased on the seventh day of streptomycin therapy.

This series also shows the extensive range of surgery that can be performed with impunity if an agent such as streptomycin is at hand to eliminate serious complications. In the patients who failed to respond to therapy further surgery in conjunction with the antibiotic may secure a satisfactory result.

## CONCLUSIONS

The keynote of successful treatment of tuberculous sinuses and abscesses, in our experience, is adequate drainage coupled with streptomycin therapy. Since the use of streptomycin, incision of abscesses can be performed without fear of added risk to the patient. It is advisable, but not imperative, to institute streptomycin therapy two or three days before incision and drainage. In this group of patients we did not close these abscesses after evacuation and the results obtained, if the tract is left open to drain freely, have been good. Recently we have closed several abscesses after evacuating the pus and removing the necrotic debris and bone with excellent early results.

In an effort to determine the optimum dosage to bring about healing

TABLE 5  
GENERAL CUTANEOUS SINUSES AND FISTULAS

Type	Duration	Original Surgical Procedure	Adjunctive Surgical Treatment	Daily Dosage	Duration of Treatment	Healed	Remarks
Ureterocutaneous fistula	28 days	Incision and drainage of psoas abscess	None	1 gm.	100 days	20 days	On the 7th day urine could no longer be detected issuing from fistula
Postpericardectomy sinus	28 days	Pericardectomy	Resection ant pericardium	1.8 gm	60 days	28 days	Abscess found in anterior pericardium
Proctoforectal fistula	14 days	Occurred following proctoscopic biopsy		1 gm	120 days	21 days	Prostatic abscess, the Drainage ceased 7th day. Normal in size & consistency on 120th day
Postappendectomy sinus	8 yrs	Appendectomy	None	1.8 gm	120 days	83 days	
Postthoracoplasty sinus	2½ yrs.	Thoracoplasty	Excision of sinus tract	1 gm	120 days	110 days	
Dehiscence of thoracoplasty wound	5 yrs	Thoracoplasty	None	2 gm	120 days	Unhealed	Decreased in size and drainage 50% in 120 days
Thoracotomy sinus	25 days	Explorative thoracotomy	None	2 gm.	40 days	Unhealed	Resistant (50 mcg/ml) on 40th day of therapy. Streptomycin discontinued

and with the minimal amount of toxicity, we have arrived at a total dosage of 1 gm. daily in two equally divided doses, given twelve hours apart. Early in this series with a dose of 1.8 gm. to 2 gm. of streptomycin daily, a high incidence of vertigo and headache was noted. The dose at that time was given every four hours in 0.2 gm. doses. In this group three patients still show some residual vestibular damage clinically, but all have been discharged and have apparently been able to compensate fairly well. This toxic effect has not been so marked in patients receiving 0.5 gm. every twelve hours. It has been thought that toxicity is produced by the average blood level of streptomycin rather than the highest level.<sup>11</sup> By employing a smaller dose and giving it in 0.5 gm. twice daily, a high blood level is not maintained. This may explain the lower incidence of toxic reactions from the 0.5 gm. dose twice daily. We find that the speed of healing is about as fast with a daily dose of 1 gm. as with the 1.8 gm. daily dose.

The optimum duration of treatment has not been definitely determined. It has been shown that resistance to streptomycin by the tubercle bacillus tends to develop in forty-five days on the dose of 1 gm. daily.<sup>12</sup> With this fact in mind, it has been recommended by the Streptomycin Committee of the National Research Council that the duration of treatment be forty-two days using a dose of 0.5 gm. twice daily twelve hours apart. Once resistance has developed, the lesion may in some cases become worse, and the patient may not derive any benefit from the drug in the future.

We have given streptomycin over longer periods of time in this series than that recommended above. This regimen was in effect before the present technic of resistance studies was perfected. In our group of patients we have used the reaction to the drug by the patient and the healing of the sinus as our index for determining duration of therapy.

As noted previously, streptomycin is a dangerous drug. The patient must be continually observed for severe eighth nerve damage. Either of the two divisions of this nerve may be affected. The patient may experience vertigo, tinnitus or deafness. We do not believe that mild dizziness or vertigo warrants discontinuance of the drug. Most of these patients showed an eosinophilia, in one case as much as 25 per cent. In one instance the drug was discontinued after six weeks because the patient developed an exfoliative dermatitis.

### SUMMARY

1. We have reviewed a series of sixty-three patients with 134 actively draining tuberculous sinuses.
2. Of the sinuses, 126 or 94 per cent have healed.

3. Incision and open drainage of the tuberculous abscess in conjunction with streptomycin therapy was found to be the best method of treatment.

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## **STREPTOMYCIN AND SECONDARY CLOSURE IN THE TREATMENT OF TUBERCULOUS SINUSES**

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### **INTRODUCTION**

THE role of streptomycin in the treatment of tuberculosis has stimulated considerable clinical investigation since its isolation in 1943 by Schatz, Bugie and Waksman.<sup>1</sup> It is now apparent that streptomycin possesses the pharmacologic properties required of a substance to be used in this chronic disease. This new antibiotic is not uniformly effective in the treatment of all tuberculous lesions. It appears to facilitate the healing of tuberculous sinuses, heretofore refractory to therapeutic measures.<sup>2, 10</sup> Prior to the advent of streptomycin these sinuses were noted for chronicity and high recurrence rate. It is our purpose in this section to comment on the early effects of streptomycin in the treatment of these complications.

### **CLINICAL PATHOLOGY**

When tubercle bacilli are implanted in soft tissue, either by the hematogenous or lymphatic route, monocyctic and giant epithelioid cell production is stimulated.<sup>3</sup> The lipid fractions of the tubercle bacillus, especially the phosphatides, are considered the necessary factors for the multiplication and maturation of these cellular elements.<sup>4</sup> With monocyctic and giant cell production, a tubercle is formed, and a localized site of necrosis of previously healthy tissue is produced. The highly cellular inflammatory tissue invades by contiguity; bone, cartilage, and even dense fibrous tissue offer only a temporary barrier. In the active stage, the abscess contains cell debris and caseous material. The wall consists of granulation and fibrous connective tissue, permitting transudation into the cavity. As enlargement of the abscess develops, it follows a course of least resistance, but maintains a definite limiting wall. If the skin is ruptured, the contents are expelled, but the wall of tuberculous tissue may persist as a sinus as long as active disease remains.<sup>5</sup>

Tuberculous infection of the thoracic wall is not uncommon. It is

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usually associated with tuberculosis of the pleura, lungs, or other organs. The infection spreads from the lung or pleura through the lymphatics to the intercostal, internal mammary or parasternal lymph nodes; secondarily, perichondrium, costal or sternal periosteum are involved and then the skeletal structures or soft parts.<sup>6, 7, 8</sup> Pleural lymphatics also communicate with a group of retroperitoneal lymph nodes situated near the vertebral attachments of the diaphragmatic crura.<sup>8</sup> Tuberculous abscess formation at these sites is usually not a serious complication. Rupture into the pleural cavity or mediastinum is rare. However, tuberculous involvement of the thoracic wall is highly resistant to therapy.

The management of Pott's disease becomes increasingly difficult in the presence of psoas abscesses and sinuses.<sup>9-12</sup> Psoas abscesses occur in approximately 25 per cent of cases of tuberculous spondylitis.<sup>13, 14</sup> With elimination of vertebral motion by spinal fusion, paravertebral and psoas abscesses tend to disappear. In Cleveland's review, 54 per cent of the patients with Pott's disease, psoas abscess and sinuses, died.<sup>14</sup> Tuberculous sinuses predispose to secondary bacterial invasion, toxicity, amyloid disease and may delay elective operative procedures by contamination of the proposed operative field.

#### DISCUSSION OF TREATMENT

Needle aspiration is used successfully in treating localized as well as extensive abscesses. To avoid the formation of a sinus tract, a large needle should be introduced into the skin about 2 cm from the margin of the abscess. The needle should be directed into the normal subcutaneous tissue and then into the center of the abscess. Employing this technic, Kisch has aspirated hundreds of abscesses, some eighty to ninety times, with rare sinus tract formation.<sup>15</sup>

Konig in 1900 reported 106 cases of thoracic wall tuberculosis. He advocated radical excision and primary closure. Sixty-nine per cent of these cases healed.<sup>9</sup> Auchinloss,<sup>16</sup> Bisgard<sup>17</sup> and Herzmark,<sup>18</sup> employing this technic, also reported moderate success. However, only 37.5 per cent of the patients reviewed by Carr and Alexander healed, and Chaklin in 1937 noted that 60 per cent of his cases developed chronic draining sinuses.<sup>19</sup>

Rapidly accumulating evidence indicates the value of streptomycin in the treatment of these previously refractory tuberculous sinuses. Sound surgical procedures in conjunction with streptomycin are essential. The origin and extent of the sinus should be carefully investigated with roentgenograms and radiopaque oil. Adequate drainage of encapsulated purulent material with conversion of an abscess to a sinus is necessary before streptomycin can be used effectively.<sup>20</sup> The sinus

should be derooft, and both granulation and fibrous tissue removed. In thoracic wall tuberculosis, resection of all necrotic bone and cartilage is important. Considerable success with this therapeutic regimen has been reported by Brock<sup>20</sup> and Hinsbaw.<sup>2</sup> This constitutes a step forward in the management of the so-called "cold" or tuberculous abscess and the draining sinus.

Hinsbaw recommended 2 gm. of streptomycin for three to four months. He noted that within four to six weeks the purulent drainage either had changed in character or had ceased. If therapy was discontinued at this point, prompt reactivation of the process occurred. If there was a spontaneous closure of the sinus, and streptomycin was continued for a period of weeks thereafter, the closure was maintained. Twenty per cent of these sinuses recurred and continued to drain. In Brock's recent series, 85 per cent of sixty sinuses treated therapeutically with 1.8 gm. of streptomycin required six to twenty weeks to close. Even when streptomycin is used in the above fashion, healing is slow.

The results at this institution with streptomycin and open surgical management were similar to those of Hinsbaw and Brock. Twelve patients with seventeen tuberculous sinuses were treated. Each received two intramuscular injections of 1 gm. each of streptomycin daily. The sinuses involved the knee and ankle joints, cervical, subscapular, perianal and pararectal regions, a Schede thoracoplasty defect, tracts from Monaldi drainage, and tuberculous mediastinitis. Twelve or 70.5 per cent of the sinuses healed without recurrence. All the successful closures required six to twelve weeks for complete healing. Streptomycin was discontinued after sixteen weeks in four of the five failures and after eight weeks in the fifth case, because the 50 year old patient developed extreme vertigo.

Experimental and clinical investigations indicate that the tubercle bacillus develops resistance to streptomycin with such prolonged administration, although there is some evidence that drug fastness is due to the survival and multiplication of an inherently resistant strain.<sup>21, 24</sup>

In order to obviate drug resistance and toxicity we have sought means of shortening the period of streptomycin administration. At this clinic, secondary closure of tuberculous sinuses has been employed in combination with streptomycin since March 1947. In this manner chronic sinuses were closed in fourteen days. Postoperatively streptomycin was given for twenty-one days. The resulting successful secondary closure has also reduced the patient's period of hospitalization. Spinal fusion for tuberculous spondylitis was not delayed by draining sinuses in the projected site of incision. Streptomycin was administered for a short time, without apparent toxicity or bacillary resistance.

## SECONDARY CLOSURE

Prior to any actual surgical procedure, abscesses are aspirated for diagnostic smear and culture. Roentgenograms are helpful when lesions are visible, but the absence of visible lesions of bone or cartilage does not rule out tuberculosis. Even extensive lesions of the cartilages are not demonstrable roentgenographically. Stereoscopic, Bucky and tomographic roentgenograms have been found useful in localizing the source of infection. Radiopaque oil may outline communicating sinuses not previously suspected.

After the diagnosis of tuberculosis is established, the patient is prepared by giving streptomycin (1 to 2 gm. daily) intramuscularly. Here as in all problems of wound healing, the high caloric and high protein diet with supplementary vitamins is of fundamental importance.<sup>22</sup>

After one week of streptomycin preparation, the abscess or sinus is considered ready for surgical exploration. General anesthesia is employed, because local anesthesia is unsatisfactory in an infected field. All ramifications of the sinuses are deroofed with complete excision of tuberculous granulation tissue. Localized pockets of purulent material are drained adequately and dependently. If the thoracic wall is involved, diseased bone and cartilage is resected. No stump of cartilage is left at the costochondral junction or on the sternum, since such remnants may become necrotic and cause recurrence of the tuberculous process. Following adequate operative investigation of the tuberculous lesion, the open wound is then packed with iodoform gauze. This acts not only as a hemostatic agent, but also stimulates the production of healthy granulation tissue. Postoperatively the iodoform pack is removed in forty-eight hours and replaced with a dressing saturated with azochloramid. The dressings are changed frequently and the wound irrigated daily with azochloramid solution.

If the initial operative débridement is complete, wound revision and secondary closure can be undertaken after seven to ten days. Under general anesthesia, the remaining fibrotic wall is excised with minimal sacrifice of healthy tissue. The muscle and fascial planes are developed individually for closure in layers. Interrupted fine chromic catgut sutures are used in the muscle, fascia, and the subcutaneous tissue, and interrupted silk sutures in the skin. The skin sutures are removed after ten days. Streptomycin is continued for a period of twenty-one days after secondary closure, the inclusive period of therapy being thirty-five days.

**Results.**—Using these surgical procedures in conjunction with the streptomycin regimen, seventeen tuberculous abscesses and sinuses in ten patients were treated. The cases included residual Schede thoracoplasty wounds, extensive psoas and parasternal abscesses and sinuses,

periostitis of the second and third ribs, and tuberculous involvement of the sternoclavicular articulation (Figs. 485 and 486).

All seventeen secondary closures have remained healed and there have been no abscess or sinus recurrence in a follow up period of four to eight



Fig 485.—Secondary closure of a parasternal tuberculous sinus, two months after operation

months. The following clinical histories are presented as illustrative cases.

**CASE I (H. P., No 19,972)**—A 29 year old white patient was admitted to this hospital in 1944 with the diagnosis of pulmonary tuberculosis. Pneumothorax was maintained for one year, but discontinued because of bronchiectasis of the right middle and lower lobes. Right pneumonectomy was performed in November 1945. Postoperatively, the patient developed a bronchopleural fistula and a mixed empyema. In January 1946, open thoracotomy was performed to obtain more adequate drainage. A three stage nine rib right thoracoplasty was completed in February 1946. The thoracotomy wound continued to drain and a Schede thoracoplasty was performed in October. The Schede thoracoplasty wound continued to drain. Sputum cultures taken in August 1947 were positive for acid-fast bacilli. Cultures of the residual empyema pocket were also positive. Bronchoscopy re-

In this case, two extensive thoracic wall abscesses were incised and drained. One abscess was drained and secondarily closed in one week. The other was drained, with removal of granulation tissue and necrotic tuberculous lymph nodes, and then closed to heal by first intention. Both wounds healed without recurrence of abscesses or sinuses. This suggests that the use of streptomycin may render primary closure practical after the drainage and débridement of tuberculous abscesses.

In tuberculous involvement of the chest wall, the importance of removing all necrotic bone and cartilage is stressed. During operation, perforation of the parietal pleura is meticulously avoided as the resulting infection of the pleural cavity might represent a fatal complication. To prevent excessive pleural soiling, in the event of inadvertent pleural opening, the anesthetist maintains the patient on gentle constant positive pressure. The pleura is then promptly and completely closed without a pneumothorax developing. Should a pneumothorax develop in spite of these precautions, the air must be aspirated immediately.

**CASE III (J. M., No. 19, 208)**—A 29 year old white man was admitted to this hospital in June 1946 with the diagnosis of pulmonary tuberculosis. The bilateral disease improved with six months of bed rest, but an elevated temperature and sedimentation rate persisted. In February 1947 a right psoas abscess developed and aspirations were positive by smear and culture for acid-fast bacilli. Roentgenograms revealed disease of the twelfth dorsal, first and second lumbar vertebrae. The right psoas shadow was obliterated with marked upward and lateral displacement of the kidney. The abscess enlarged rapidly in spite of needle aspirations and dissected mesially to the spinous processes. Several draining sinuses also developed. Spinal fusion was delayed because of the close proximity of the abscess and sinuses to the proposed site of incision.

In March 1947 streptomycin, 2 gm. daily, was instituted and one week later, under general anesthesia, a 12 cm. incision was placed in the right lumbar region. As the lumbar dorsal fascia was approached in Petits triangle, it was necessary to aspirate 1200 cc. of purulent material. Further exploration revealed the cavity to be anteriorly several centimeters beyond the superior iliac crest, posteriorly to the transverse processes, superiorly to the hilum of the right kidney, and inferiorly into the pelvis. It was also noted that the abscess had perforated muscle fascia, so that the anterior wall was composed of retroperitoneal ascending colon and thickened peritoneum. Mesially the quadratus lumborum and psoas muscles were necrotic and totally destroyed. Postoperatively, the large sinus was frequently repacked with iodoform gauze and azochloramid dressing. The wound was secondarily closed in May 1947 and three weeks later a Hibbs spinal fusion of the eleventh dorsal to the third lumbar vertebrae was performed. Streptomycin was discontinued in July.

All wounds remained healed and the patient was discharged from the hospital in December 1947.

In this instance the location of the drainage site rendered spinal fusion hazardous. Even with streptomycin, the wound continued to discharge

for eight weeks after the initial incision. It was apparent that complete healing would be long. The abscessed space beneath the skin and above the spinous processes had obliterated, but the continued drainage from the incisional site precluded the adjacent clean operation of spinal fusion. Thus, secondary closure of the sinus was attempted to produce the essential clean skin area for spinal fusion. The secondarily closed wound

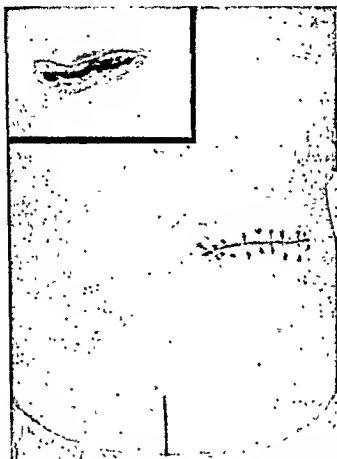


Fig. 488 —Preoperative and postoperative views of a right psoas tuberculous sinus

healed firmly and the spinal fusion was carried out through an incision but 3 cm. distant. There were no complications and the patient was discharged from the hospital six months later.

This was the first secondary closure performed at this institution. The success helped formulate our present policies concerning the use of streptomycin and secondary closure in the treatment of tuberculous abscesses and sinuses. Since this original success, there have been four additional similar cases and no failures. It would appear that short periods of streptomycin administration (about thirty-five days) are adequate (Fig. 488).



## CONCLUSIONS

1. The management of thirty-four tuberculous abscesses and sinuses in twenty-two patients is presented.

2. Seventeen sinuses in twelve patients were treated by surgical drainage, débridement and 2 gm. of streptomycin daily. Twelve or 70.5 per cent healed in six to twenty weeks. There have been no recurrences.

3. Sixteen abscesses and sinuses in ten patients were treated by surgical drainage, débridement and secondary closure.

a. Five patients with eight lesions received 2 gm. of streptomycin daily for eight to sixteen weeks.

b. Five patients with eight lesions received 1 gm. of streptomycin daily for two weeks prior to secondary closure, and three weeks following operation.

All wounds secondarily closed healed firmly without recurrence. Streptomycin in a dose of 1 gm. daily for five weeks appears adequate.

4. Primary closure, after drainage and débridement, of a tuberculous parasternal abscess with streptomycin was successful.

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## THE TREATMENT OF URINARY AND GENITAL TUBERCULOSIS WITH STREPTOMYCIN

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OLIVER STONINGTON, M. D.

THE tuberculous process in the urinary tract begins in the kidney. The renal lesion, once demonstrable clinically, has a definite tendency to progress and only very rarely heals spontaneously. This is largely due to the early formation of tuberculous calyceal and ureteral strictures which produce a stasis of tuberculous urine in the kidney.

Conservative medical management which is so effective in certain forms of pulmonary tuberculosis has proved very disappointing in renal tuberculosis. In fact, bed rest is harmful because it enhances urinary stasis.

A cure following nephrectomy for unilateral renal tuberculosis depends upon the subsequent spontaneous healing of lesions in the remaining stump of the ureter and bladder. In such cases lesions are almost always present in the genitalia and in other organs in the body even though they may not as yet be demonstrable clinically. These lesions also must heal spontaneously if a cure is to be accomplished. That this often happens is proved by the fact that nephrectomy in unilateral renal tuberculosis is followed by a cure in 50 to 55 per cent of the cases, whereas failure to remove the kidney almost invariably leads to death within five years.

In 45 to 50 per cent of the cases, however, the condition progresses in spite of nephrectomy, and a fatal outcome occurs, often after a long period of intense misery.

The earlier cases offer a better chance of a cure following nephrectomy. In fact, in the earliest forms in which the renal lesion consists mainly of a small caseous ulcer on the summit of a single renal papilla, the possibility of a cure following nephrectomy is better than 90 per cent. Failure to remove the kidney at this stage almost invariably leads to progression of the lesion and a loss of the best and sometimes the only opportunity to achieve a cure. It requires great courage on the part of the surgeon to remove a kidney with a normal function, with normal

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pelvic contours, and which, except for the presence of a minute lesion, is otherwise normal. Theoretically such a case would seem to be ideal for conservative management. The fact that the symptoms at this stage are often minimal or even undergo complete remission for a time leads to a false feeling of security; hence, conservative management is usually employed with disastrous end results.

It is obvious from a consideration of the above mentioned facts that nephrectomy, although it has up to the present been the most effective weapon at our command, leaves much to be desired.

Conservative medical management, which has been so disappointing in the past, will eventually prove to be the ideal method of treatment, and it awaits only the discovery of an antibiotic of sufficient potency completely to destroy the tubercle bacillus. The discovery of streptomycin raised the hope that this might be the long awaited agent. Although subsequent investigations revealed that this was not the case, the use of this new antibiotic has proved to be a definite step forward in the treatment of urinary tuberculosis and genital tuberculosis in the male.

#### THE RESULTS OF STREPTOMYCIN THERAPY

In an attempt to evaluate its effectiveness, twenty-three patients with urinary and genital tuberculosis were treated with streptomycin, in daily doses of 1 gm. (in two divided doses of 0.5 gm. each) for a period of 120 days. Each patient received a complete urinary study before treatment and at intervals of one month during and after treatment. Sixteen patients have completed their full course of streptomycin and have been observed for periods of one to eight months following completion of the therapy.

Among thirteen cases with renal involvement nine were bilateral and four were unilateral. Ten of these patients had genital lesions. In three additional cases the disease was limited to the genitalia. The results may be summarized as follows:

**The Kidney and Ureter.**—In nine kidneys with positive pyelographic evidence of tuberculosis the bacteriological findings became negative in three. In five the pyelograms showed no change after treatment and in four definite progression was noted. In one of these the kidney underwent rapid hydronephrotic dilatation and became functionless during the period of treatment, due to ureteral atresia resulting from fibrous healing of tuberculous ureteral lesions.

Six of the kidneys in this group were subsequently removed. In all a very definite healing effect was noted but this was so far short of complete obliteration of the disease as not to be of clinical significance. The most

pronounced healing effect was seen on the mucous membranes of the calyces, pelvis and ureter.

The most striking results were seen in the ten patients with tuberculous kidneys showing normal pyclograms. One of these could not be catheterized for follow-up study, but in the remaining nine the bacteriologic findings became negative, and there was an appreciable reduction of the leukocyte count of the urine specimen obtained by ureteral catheter. The possibility of a cure, although very strong in this group of cases, can only be evaluated by a five to ten year follow-up study.

**The Urinary Bladder.**—Eleven patients showed involvement of the bladder. In seven definite specific lesions were identified (tubercles, ulcers, granuloma). In the remaining four the lesions were more inflammatory in appearance. In five cases the bladder returned to normal after treatment, four were improved, one remained the same, and one was worse.

The symptomatic improvement was most pronounced in these cases. Six patients had had severe symptoms with reduced bladder capacity. After treatment the capacity was increased in four, remained the same in one, and decreased in one.

Definite improvement was usually noted after four to six weeks of treatment.

The lesions in the bladder have a tendency to recur after the cessation of streptomycin therapy if the offending kidney has not previously been removed.

**Genital Tuberculosis.**—Twelve patients had genital involvement. The results in this group were not very encouraging. Significant improvement in lesions of the prostate, seminal vesicles, and epididymides, as demonstrated by rectal and scrotal palpation, did not occur after streptomycin therapy. In two patients there was a slight to moderate decrease in the size of the epididymis. Seven epididymides were removed and upon pathological study showed extensive caseous disintegration. In one of these definite progression with involvement of the testis occurred during therapy. Lesions in the prostate and seminal vesicles also progressed. Five months after epididymo-orchicectomy the rectal findings had returned to normal.

Scrotal abscesses were present in three patients. These progressed or showed no change under streptomycin therapy alone, however, after incision during therapy they promptly healed without fistula formation.

In one case bilateral scrotal fistulas and partial extrusion of the left testis were present following bilateral epididymectomy. Prompt healing followed the administration of streptomycin.

pelvic contours, and which, except for the presence of a minute lesion, is otherwise normal. Theoretically such a case would seem to be ideal for conservative management. The fact that the symptoms at this stage are often minimal or even undergo complete remission for a time leads to a false feeling of security; hence, conservative management is usually employed with disastrous end results.

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## STREPTOMYCIN AND SURGERY IN ANORECTAL TUBERCULOSIS

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### INCIDENCE AND ETIOLOGY OF ANORECTAL TUBERCULOSIS

VARIOUS medical authors give varying figures as to the incidence of anorectal tuberculosis in the general population and in tuberculous patients. The consensus is that few of all anorectal infections and fistulas are tuberculous but most of such conditions in tuberculous patients are tuberculous. Buie,<sup>1</sup> in 1938, on the basis of a study of 1772 cases of anal fistulas at the Mayo Clinic, stated that 0.7 per cent and Granet,<sup>2</sup> in 1940, declared that 0.5 to 0.6 per cent of the general population have tuberculous anorectal abscesses and fistulas. According to the latter author 5 to 11.7 per cent of tuberculous patients suffer from anorectal abscesses and fistulas. Martin,<sup>3</sup> in 1946, declared that 7 per cent of tuberculous patients have anorectal fistulas but 72 per cent of such fistulas are tuberculous.

From these figures it would appear that anorectal conditions occur approximately ten times more frequently in tuberculous patients than nontuberculous persons. However, Jackman and Buie,<sup>4</sup> in 1946, reported their analysis of 600 cases of anal fistulas at the Mayo Clinic and stated that 7 to 8 per cent of anal fistulas in a general hospital or clinic are tuberculous and in nearly all instances in which they are unmistakably tuberculous there is a focus elsewhere in the body. They found 88.5 per cent of their cases had no tuberculosis, either in the fistula or elsewhere in the body, while 11.5 per cent did show evidence of tuberculosis somewhere in the body.

Although the consensus is that the tubercle bacillus is always or almost always a secondary invader in anorectal tuberculosis,<sup>1, 2, 5, 6, 7, 8, 9</sup> Jackman and Buie commented that they were unable to answer whether the tubercle bacillus is a primary or a secondary invader of anal fistulas and pointed out that in eleven of their cases no tuberculous focus could be found elsewhere in the body yet guinea pig inoculation and/or histopathologic examination of the fistula were positive. They stated that, as nearly as they could determine, the fistulas in this small group

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Feldman and Hinshaw<sup>19</sup> in 1947. Extensive investigations of the use of streptomycin in the treatment of tuberculosis in man and considerable experimental research on animals have been and are being carried out. Experience thus far has demonstrated that this antibiotic agent is beneficial in the treatment of certain types of human pulmonary and nonpulmonary tuberculosis but that it should not be used to replace but rather as an adjunct or supplement to other recognized methods of therapy.<sup>20, 21</sup> Recently Corper and Cohn,<sup>22</sup> on the basis of experimental studies, stated that streptomycin cannot be considered a cure for tuberculosis since it will not destroy virulent human tubercle bacilli, nor will it completely retard their development *in vivo*, nor will it prevent a lethal issue of tuberculous infection although it will retard such issue. They conclude from experimental evidence that streptomycin is no more than an incomplete retardant of tuberculosis in man. Bogen,<sup>23</sup> however, in discussing this article, declared that he and his associates had many guinea pigs surviving after treatment with streptomycin whereas the controls died many months before.

For some time the Surgical Service at this hospital has advocated and practiced the same surgical treatment for tuberculous abscesses and sinuses, with and without associated tuberculosis of bone, as for non-tuberculous abscesses and sinuses, namely, incision with adequate drainage, or excision. Observing the excellent results obtained from the treatment of tuberculous abscesses and sinuses with this method supplemented by streptomycin therapy, it was decided to utilize the same regimen in anorectal tuberculosis when streptomycin became available for such use. A series of twenty-seven cases of anorectal tuberculosis treated with streptomycin, in the majority of which the drug was used as a supplement to definitive surgical incision and drainage or excision, comprises this study. Surgical incision or excision was performed if feasible in all cases unless the patient's pulmonary disease or some other condition contraindicated the procedures or rendered them inadvisable. At operation the wounds in the later cases were packed with oxidized gauze (oxycel) for hemostasis and all wounds postoperatively were kept clean and free of adhesions by swabbing with plain gauze or cotton applicators every other day. For a varying period of time the wounds were packed loosely with gauze impregnated with furacin ointment. Care was taken to assure proper and satisfactory healing from within to the outside.

Except for the first four patients, who received 1.8 to 2 gm. daily, streptomycin was administered intramuscularly in a daily dosage of 1 gm. for a maximum period of approximately 120 days or until expiration of

thirty days after complete healing. Under the recently adopted protocol, streptomycin will be administered until healing is complete or for a maximum of forty-two days, whichever occurs first. Forty-two days have been specified as the maximum period of treatment because it has been determined that in the average patient the organism becomes resistant to the drug in about forty-five days.

**Results.**—The results obtained in the series of twenty-seven cases of anorectal tuberculosis treated with streptomycin with and without surgery are reported in detail in Table 1. The classification and activity of the pulmonary tuberculosis was "active, far advanced" in twenty-four cases and "active, moderately advanced" in the other three. The duration of the anorectal tuberculosis prior to definitive surgical incision or excision and/or streptomycin therapy varied from four days to as long as seven years. In eleven of the cases one or more prior proctologic surgical procedures had been performed without accomplishing cure. In twenty-five cases one or more bacteriologic and histopathologic examinations were positive for tubercle bacilli. Of the other two cases, in one (Case 3), the histopathologic report was consistent with tuberculous etiology but not diagnostic although clinically the condition appeared tuberculous and had resisted treatment for seven months and in the other (Case 23) the histopathologic report was "probably tuberculous" but not conclusively diagnostic.

As shown in Table 2, the smear was positive in only two cases, the guinea pig inoculation positive in eight cases, the culture positive in fifteen cases and histopathologic examination positive in nineteen of the twenty-four cases in which biopsies were taken, one of which was "probably tuberculous." In two additional cases the histopathologic report was "possibly tuberculous but not diagnostic." Acid-fast bacilli were found microscopically in the pathologic section in thirteen of the nineteen cases.

Toxic reactions occurred in only seven cases or 25.9 per cent as manifested by vertigo in six patients, one of which also had a transient pruritic papular dermatitis, and the other patient developed an elevated blood nonprotein nitrogen and granular casts in the urine necessitating discontinuance of the drug. A "healed" result was obtained in twenty-three cases, or 85.2 per cent, and improvement in the other four cases or 14.8 per cent, with maximum improvement in one case and slight and probably temporary improvement in the remaining three. In the twenty-seven cases definitive surgical incision or excision supplemented by streptomycin therapy was performed in nineteen cases or 70.3 per cent with resultant complete healing in all. In the eight cases in which streptomycin was administered without definitive surgical incision or

TABLE 1.—CLINICAL RESULTS FROM STREPTOMYCIN THERAPY WITH AND

Case	Pulm TB, Classification	Anorectal Condition			Surgical Treatment (Other than Biopsy)
		Diagnosis	Duration	Previous Therapy	
1*	FA, active	Fistulas, anal & perianal fistulas, multiple (5), tuberculous	6 yrs	I & D 1941 I & D 1943	Excision of fistulas 11/15/45
2	FA, active	Sinus, perianal, residual of excision operation, tuberculous	8 mos	Excision of anal ulcer 5/2/45	None
3*	MA, active	Ulcer & sinus, residual of fistulectomy. Clinically tuberculous	6 mos	Fistulectomy 7/30/45	Incision of sinus 1/10/47
4*	FA, active	Fistula, anal, tuberculous	13 mos	I & D of perianal abscess Sept 1945	Fistulectomy 11/20/45
5	FA, active	Ulcer & fissure, perianal, tuberculous	2 mos	None	None
6*	MA, active	Abscess, perirectal, & ulcer, rectal, secondary to TB of prostate	15 mos	None	I & D of abscess with biopsy forceps 2/1/47
7	FA, active	Radial ulcers, rectal & perianal, residual of excision of 2 anal fistulas, tuberculous	13 mos	Excision of 2 anal fistulas 6/24/45	None
8*	FA, active	Abscess perianal, tuberculous	Not known	None	I & D of abscess 7/29/47
9*	MA, active	Abscess & sinus, perianal, tuberculous	6 mos	I & D of perianal abscess 4/30/47	Excision of abscess & sinus 9/2/47
10*	FA, active	Abscess, perianal, tuberculous	1 month	None	I & D of abscess 7/10/47
11*	FA, active	Fistula, anal, ulcer, perianal abscess, rt buttocks & ulcer, rectal, tuberculous	4 yrs	None	I & D of abscess & partial excision of ulcer 9/25/47 Fistulectomy & excision of residual abscess 1/30/48

## WITHOUT SURGERY IN TWENTY-SEVEN CASES OF ANORECTAL TUBERCULOSIS

Streptomycin Therapy				Results		Mos. Since Healed	Remarks
Duration	Wks.	Dosage Daily (gm.)	Toxicity	Healed	Other		
6/27/46 to 9/26/46 10/26/46 to 12/24/46	13 8½	1.8 1.8	None	Yes 4/18/47	—	8	Discharged arrested 12/20/47. Healed. No follow-up.
1/30/47 to 2/25/47	4	1.8	None	Yes 2/10/47	—	14	Discharged arrested 4/7/48. Healed. Streptomy- cin supplement- al to pneumonectomy.
2/10/47 to 5/10/47	13	2.0	Severe vertigo, tinnitus & ataxia	Yes 4/14/47	—	6	Discharged AWOL 10/12/47, MA, active Healed. No follow-up.
2/11/47 to 5/12/47	15½	2.0	Severe vertigo & ataxia	? healing 1/30/47. Remained healed	—	5½	Disciplinary discharge 7/25/47, FA, active Healed. Streptomycin given for other extra- pulmonary TB. No follow-up.
6/ 9/47 to 10/ 7/47	17	1.0	None	Yes 8/13/47	—	2½	Discharged AWOL 10/18/47, FA, active Healed. No follow-up.
6/16/47 to 10/20/47	10½	1.0	None	Yes 10/14/47	—	1	Discharged AWOL 11/10/47, MA, active Healed. No follow-up.
8/ 1/47 to 12/ 1/47	17½	1.0	None	—	Max imp Almost healed	—	Rehab. One ulcer com- pletely healed. Site of other ulcer almost healed. Clean denuded scar tissue.
5/ 9/47 to 12/16/47	20	1.0	Mild vertigo	Yes 12/26/47	—	1½	Became psychotic. Transferred NP Hosp 2/13/48 FA, active. Healed Streptomycin, given for GU TB. No follow-up.
8/23/47 to 12/ 5/47	14	1.0	None	Yes 10/10/47	—	4	Discharged AWOL 2/14/47, MA, active. Healed. No follow-up.
8/28/47 to 11/ 8/47	10½	1.0	None	Yes 9/22/47	—	8½	Hospitalized, FA, ac- tive. Healed.
10/24/47 to 4/12/48	24½	1.0	Severe vertigo & ataxia	Yes 8/29/48	—	2	Hospitalized, FA, act., imp., Almost healed 4/12/48. Completely healed 5/20/48. Sputum converted.

TABLE 1—

Case	Pulm TB, Classification	Anorectal Condition			Surgical Treatment (Other than Biopsy)
		Diagnosis	Duration	Previous Therapy	
12	FA, active	Fistulas, anal, multiple (3), tuberculous	4 yrs	I & D of perianal abscess & incision of fistulas 6/23/47	None
13*	FA, active	Abscess & sinus, perianal, tuberculous	4 mos	I & D of perianal abscess 9/4/47	I & D of abscess & sinus 11/5/47
14*	FA, active	Abscess & sinuses, multiple (2), perirectal, tuberculous	5 mos	None	I & D of abscess & sinuses 11/17/47
15*	FA, active	Abscess & sinus, perianal, tuberculous	4 days before I & D 5 mos before streptomycin	None	I & D of abscess 7/12/47
16	FA, active	Abscess, ulcer & sinus, perianal, tuberculous	14 mos	I & D of perianal abscess Oct 1946	None
17*	FA, active	Sinuses, perianal, multiple (2), tuberculous	6 yrs	Repeated I & D (overseas) Fistulectomy 1943	Excision of sinuses (conservative) 1/13/48
18*	FA, active	Fistulas, anal, (2) ext openings, & abscess, perianal, tuberculous	1 yr	None	Fistulectomy & I & D of abscess 1/15/48
19*	FA, active	Fistula, anal, & abscess, perianal (coccygeal region), tuberculous	7 yrs	None	Fistulectomy & excision of abscess 1/13/48
20*	FA, active	Fistula, anal, & abscess, perianal, tuberculous	5 mos	None	Fistulectomy, I & D of abscess & partial hemorrhoidectomy 3/10/48
21	FA, active	Fistula & ulcer, rectal, & abscess, perirectal, tuberculous	3 yrs	Operations for rectal fistula Dec 1944 & Apr 1945	None
22*	FA, active	Abscess, perianal, tuberculous	6 days	None	I & D of abscess 11/15/47

Continued

Streptomycin Therapy				Results		Mos Since Healed	Remarks
Duration	Wks	Dosage Daily (gm)	Toxicity	Healed	Other		
7/21/47 to 9/20/47 11/12/47 to 1/16/48	9 9½	1.0 1.0	Elevated NPN (40.5), granular casts in urine	—	Slight impr 1 fistula closed, 2 fistulas persist	—	Hospitalized, FA, active Only slight drainage Streptomycin disc't because of elevated NPN & organism resistant
11/15/47 to 2/18/48	13½	1.0	None	Yes 1/19/48	—	1½	Discharged AWOL 2/28/48, FA, active Healed. No follow-up
12/ 8/47 to 4/ 5/48	17	1.0	None	Yes 3/18/48	—	2½	Hospitalized, FA, active Healed
12/23/47 to 4/20/48	17	1.0	None	Yes 2/2/48	—	4	Hospitalized, FA, active Healed Streptomycin pulmonary protocol.
1/ 6/48 to 2/27/48 (died)	7½	1.0	None	Yes 2/2/48	—	½	Died of FA Pulm TB 2/27/48. Streptomycin laryngeal protocol Healed at death
1/19/48 to 3/18/48	8½	1.0	None	Yes 2/11/48	—	3½	Hospitalized, FA, active Healed
2/ 1/48 to 3/19/48	7	1.0	None	Yes 2/14/48	—	3½	Hospitalized, FA, active Healed
2/ 4/48 to 3/ 1/48 Refused treatment	3½	1.0	Psychoneurotic exaggeration of vertigo & ataxia Pruritic papular dermatitis, subacute	Yes 2/27/48	—	3½	Hospitalized, FA, active Healed
2/ 6/48 to 6/ 5/48	17	1.0	Slight vertigo	Yes 5/13/48	—	½	Hospitalized, FA, active Healed.
6/ 4/47 to 10/ 2/47 2/ 6/48 to 6/ 5/48	17 17	Not known 1.0	None	Yes 5/29/48	—	½	Hospitalized FA, active 1st course streptomycin-laryngeal protocol—stopped drainage but drainage recurred Insufficient obs.
2/17/48 to be disc'n't 6/15/48	15½ to date	1.0	None	Yes 6/1/48	—	½	Hospitalized, FA, active Healed.

TABLE 1—

Case	Pulm TB, Classification	Anorectal Condition			Surgical Treatment (Other than Stompy)
		Diagnosis	Duration	Previous Therapy	
23	FA, active	Fistula, anal, horseshoe type, & ulcer, rectal, probably tuberculous	4 yrs	None	None
24*	FA, active	Abscess, perianal, tuberculous	3 wks	None	I & D of abscess 11/29/47
25*	FA, active	Fistula, anal, tuberculous	1 mo	None	Fistulotomy 2/20/48
26	FA, active	Sinus & abscess, perianal (isorectal region), tuberculous	3 yrs	None	None
27*	FA, active	Abscess, perianal, tuberculous	4 days	None	I & D of abscess 3/7/48
Total and Percent	24 FA 3 MA		4 ds to 1 yr	11	19 79%

FA, MA = far advanced, moderately advanced

I &amp; D = Incision and drainage

\* Treated both by operation and streptomycin

excision only four, or 50 per cent, healed while in the other four cases maximum improvement was secured in one and slight improvement in three

Although a tuberculous anorectal condition may rarely heal spontaneously and medical writers at times make broad statements to the effect that, if proper and adequate surgery is performed, anorectal tuberculosis will usually heal, it is well known that if healing occurs it is delayed in comparison with nontuberculous conditions and in an appreciable percentage of cases this type of tuberculosis will not heal in spite of proper and adequate surgery or if it heals it will recur later. At this hospital during the period of the cases reported, surgery alone, without supplemental streptomycin therapy, was performed in two cases of tuberculous

## Concluded

Streptomycin Therapy				Results		Moa Since Healed	Remarks
Duration	Wks	Dosage Daily (gm.)	Toxicity	Healed	Other		
2/26/48 to be discon't 6/25/48	14½ to date	1.0	None	—	Slight imp	—	Hospitalized, FA, active Drainage markedly decreased. Fistula & ulcer persist.
3/ 8/48 to be discon't 6/12/48	14 to date	1.0	None	Yes 5/13/48	—	1	Hospitalized, FA, active Healed
3/11/48 to be discon't 6/23/48	16 to date	1.0	None	Yes 5/29/48	—	1	Hospitalized, FA, active Healed.
4/ 1/48 to 5/14/48	6	1.0	None	—	Slight imp	—	Hospitalized, FA, active Streptomycin incidental to open pneumonolysis. Sinus closed 5/21/48 but reopened 5/29/48, Drainage decreased.
12/ 3/47 to 12/23/47	3	1.0	None	Yes 5/26/48	—	1	Hospitalized, FA, active 1st course streptomycin supplemental lobectomy. Healed
5/11/48 to 6/ 5/48	4	1.0					
27 100%	3½ to 24½	—	7 25.9%	23 85.2%	4 imp 14.8% (1 max imp, 3 slight imp)	—	—

anal fistula and in four cases of tuberculous perianal abscess with apparent healing in five cases but unsuccessful result in the sixth case. To date there has been no recurrence in the "healed" cases. The fact that prior surgery had been performed without success or with recurrence after apparent healing in eleven of the reported cases is indeed significant. Garnet,<sup>2</sup> in 1940, reported sixty-eight cases of perianal infections treated by radical surgical excision, with resultant healing in 72 per cent (forty-nine cases) but healing did not occur until after four months or more in fourteen instances. He stated that the following authors had also reported the following percentages of cures from surgery alone: Martin, 87 per cent; Berry, 72 per cent; and Chisholm, 98 per cent. However, careful study of the reference given as authority for Chisholm's results fails to reveal any mention of percentage of cures.

In the nineteen cases reported herein in which streptomycin and defin-



TABLE 2

BACTERIOLOGIC AND PATHOLOGIC EXAMINATIONS IN TWENTY-SEVEN CASES OF  
ANORECTAL TUBERCULOSIS TREATED BY STREPTOMYCIN THERAPY WITH  
AND WITHOUT SURGERY

Case	Smear	Culture	Guinea Pig Inoculation	Biopsy Histologi- cally Tuberculous	Acid-Fast Bacilli Found
1*	(No examinations prestreptomycin) Neg	Neg	None	Yes	No
2	None	None	None	Yes	No
3*	Neg	Neg	Neg	Possible Not diagnostic	No
4*	None	None	None	Yes	Yes
5	Neg	Pos	None	Yes	Yes
6*	Neg	Pos (pus and biopsy)	Neg	Yes	No
7	Neg	Pos	Neg	Possible Not diagnostic	No
8*	Neg	Pos	None	None taken	—
9*	Neg	Neg	Pos	Yes	No
10*	Pos	Pos	Pos	Yes	Yes
11*	Prior to streptomycin Neg	Pos	None	Yes	Yes
	During streptomycin Neg	Neg	None	Yes	No
12	Prior to 1st course of streptomycin None	None	None	Yes	No
	After 1st course of streptomycin Neg	Neg	Neg	None taken	—
13*	Neg.	Pos	None	Yes	Yes
14*	Neg.	Neg	Pos	Yes	Yes
15*	Neg.	Pos	Neg	No	No
16	Neg	Neg	Neg	Yes	Yes

TABLE 2—concluded

Case	Smear	Culture	Guinea Pig Inoculation	Biopsy Histologically Tuberculous	Acid-Fast Bacilli Found
17*	Neg	Neg	Neg	Yes	Yes
18*	Neg	Neg.	Neg	Yes	Yes
19*	Neg	Pos	Neg	Yes	Yes
20*	Neg	Neg	Pos.	Yes	Yes
21	Neg	Pos	Pos	No	No
22*	Neg	Pos	Pos	Yes	Yes
23	Neg	Neg	Neg	Yes (probably)	No
24*	Neg	Pos	Pos	No	No
25*	Neg	Pos	Pos	Yes	Yes
26	Pos	Pos	None	None taken	—
27*	Neg	Pos	Neg	No	No
Total	2 Positive	15 Positive	8 Positive	19 Positive	13 Positive

\* Treated both by operation and streptomycin.

itive surgery were combined, healing in general was comparatively prompt except in Cases 1, 6, 11, 15, 22 and 24. In Case 1 the patient had received a prior thirteen weeks' course of streptomycin terminated only one month prior to surgery combined with a second course of streptomycin. In the light of present knowledge, the organism in all probability had become resistant to the drug. Case 6 was a perirectal abscess secondary to tuberculosis of the prostate and streptomycin was not administered until nineteen weeks after incision and drainage of the abscess. In Case 11 no attempt was made to treat surgically the anal fistula until fourteen weeks after starting streptomycin, to determine the effect of the drug alone. In Cases 15, 22 and 24 streptomycin was not administered until twenty-three, twenty-three and a half and fourteen weeks respectively after surgery owing to delay in obtaining a positive bacteriologic or histopathologic examination to satisfy the requirements of the strepto-

mycin protocol. In several other cases a similar but shorter delay occurred and if it had been possible to administer streptomycin more promptly the period required for healing would probably have been shortened. Also, in Case 4, questionable healing had already occurred as the result of surgery prior to the administration of streptomycin. If these seven cases are deleted the period required for complete healing after definitive surgery was twenty-nine to 150 days or an average of 10.7 weeks, and after commencing streptomycin the healing period was thirteen to 139 days or an average of 7.8 weeks. In the case which required 150 and 139 days after surgery and starting streptomycin respectively (Case 8) the patient was prepsychotic and refused to cooperate in the postoperative treatment. In fact, this patient eventually had to be transferred to a neuropsychiatric hospital for treatment of a definite psychosis.

The results obtained in these nineteen cases in which definitive surgical incision or excision, supplemented by streptomycin therapy, was performed, are significant and most gratifying since complete healing occurred in 100 per cent with no recurrence. It is believed that the use of streptomycin supplemental to surgery is of definite value in the treatment of anorectal tuberculosis in that it increases the percentage of permanent cures, shortens the period required for healing, reduces or practically eliminates purulent discharge after a week to ten days and produces healthier granulation tissue postoperatively. Streptomycin therapy also is protective against spread or exacerbation of the pulmonary tuberculosis during surgical treatment.

Under streptomycin protection a less extensive proctologic surgical procedure may be performed with an excellent prospect of cure in selected cases in which a more radical procedure is contraindicated or deemed not advisable. For instance, it has been found that fistulotomy instead of fistulectomy has resulted in complete healing in cases of extensive anal fistulas and perianal sinuses where the more radical procedure would have necessitated severance of the internal anal sphincter and a large gaping wound. If surgery is contraindicated or not deemed advisable, streptomycin therapy alone may be administered with possible cure but the results will not be as gratifying as when surgery is supplemented by such therapy. In Cases 2 and 21 streptomycin alone closed a tuberculous perianal sinus and a rectal fistula, although the latter has not been observed long enough to be certain that healing will be permanent. However, in two other cases (1 and 11) streptomycin alone failed to close anal fistulas after prolonged treatment whereas the fistulas did close and heal after surgical excision. In three other cases (12, 23 and 26) streptomycin alone also failed to close the fistulas and these

persist. In tuberculous ulcers complete healing if it occurred under streptomycin therapy was a prolonged process and therefore it is believed that excision of this type of lesion whenever feasible would probably increase the chances of success and shorten the period of healing.

### SUMMARY AND CONCLUSIONS

1. A series of twenty-seven cases of anorectal tuberculosis treated with streptomycin with and without definitive surgery has been reported with most gratifying results.

2. Streptomycin therapy supplemental to surgical incision or excision is believed to be effective in healing anorectal tuberculosis. One hundred per cent of the cases so treated in the series reported were healed. Streptomycin should be used not to replace but as an adjunct to recognized proctologic surgical procedures. Neither should it replace proper and meticulous postoperative treatment which is of great importance and should not be neglected.

3. In selected cases in which surgery is contraindicated or deemed inadvisable, streptomycin therapy alone may be utilized with some promise of success but the results will not be as gratifying as where surgery and streptomycin are combined.

4. Streptomycin therapy makes possible in certain cases the performance of a less extensive surgical procedure than formerly would have been justified.

5. Streptomycin therapy enables the surgeon to institute surgical treatment of anorectal tuberculosis at an earlier stage in the hospitalization and treatment of the patient with pulmonary tuberculosis and serves as a protection against spread and exacerbation of the pulmonary disease during surgical treatment.

6. It is believed that streptomycin therapy supplemental to surgery definitely shortens the postoperative period required for healing and will prevent recurrence. There has been no recurrence in the cases so treated.

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## **STREPTOMYCIN THERAPY IN ORTHOPEDIC TUBERCULOSIS**

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THE diagnosis of tuberculosis of bones and joints always presents a serious problem of prolonged therapy, progressive disability and considerable expense. It is distressing to reflect that every instance of orthopedic tuberculosis represents a failure of prevention, and, too often, a failure of early diagnosis. Although this form of tuberculosis is among the oldest known afflictions of the skeletal system which has been carefully observed and evaluated, very little progress has been made in its treatment.

Any possibility of improvement in therapy justifies critical study. The early reports of streptomycin showed promise. In June 1946 the Veterans Administration began a joint investigation to determine the merits of streptomycin in human tuberculosis therapy. In Hines Hospital this program was under the direction of a local streptomycin committee headed by Dr. Arnold Shamaskin. After this general program was in operation for several months, a somewhat more detailed study directed to the special problem of tuberculosis of bones and joints was begun in February 1947. In addition to the members of the streptomycin committee, an orthopedic consultant and orthopedic residents were assigned to make a special survey and follow-up program of these cases. It is quite obvious that a number of years will be required before any definite conclusion can be presented. Nevertheless, it was felt that the relative uniformity of results observed in our twenty-two cases and the paucity of reports in the literature indicate that our observations should be more widely known.

The background and plan of investigation has been clearly presented in Veterans Administration Technical Bulletin TB 10-34—August 5, 1947. In the selection of cases it was agreed:

A. That all cases would be observed for at least sixty days prior to the initiation of streptomycin treatment, and of these, only such cases as failed to make satisfactory improvement under commonly accepted methods of therapy would be considered.

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B. That the diagnosis of tuberculosis be substantiated by positive guinea pig inoculation and cultures, or in inaccessible tuberculosis such as tuberculous spondylitis, that unequivocally positive roentgenologic findings be required to corroborate the diagnosis

C. That moderately advanced or far advanced disease would be accepted provided that the life expectancy was at least twelve months

D. That patients during therapy remain on substantially the same daily regimen including physical activity during streptomycin therapy as had been maintained prior thereto.

E. That no additional innovations in therapy be initiated during the course of streptomycin treatment.

These patients were observed and treated concurrently with a substantially similar group that did not receive streptomycin

At the onset of the orthopedic study the routine dosage was 2 gm. of streptomycin intramuscularly every twenty-four hours. This was divided as follows: 0.4 gm. was injected at four hour intervals from 8 A. M. to midnight, the 4 A. M. dose being omitted for the convenience of the patient and nursing staff

Detailed observation of the patient was made before and during the treatment to protect him and provide essential information. An attempt was made to keep these observations simple, but they did prove very burdensome.

The streptomycin investigation began with Dr. Bradley Carr as the resident in charge until June, when part of this work was taken over by Dr. Edward Millar. Although patients with orthopedic tuberculosis are on several different services, they are seen by the same orthopedic consultant and the streptomycin committee

#### CASE STUDY

At present we are presenting a brief survey of twenty-two cases. They included: spinal (four dorsal, seven lumbar, and one sacrum), pelvic (one sacroiliac, two ilium, and one hip joint), others (four knee [one bilateral], four ankle, one shoulder, one elbow, one wrist, one phalangeal, one sternum, and two ribs.) Of this group, sixteen cases had a total of twenty-one draining sinuses, all of which closed within a period varying from ten to eighty-four days, an average of thirty-five days. Two of these patients subsequently began to drain again and required surgical treatment following the first course of streptomycin. Of the twenty-two cases, seven received daily dosages of 1 gm., and the remaining fifteen averaged 2 gm. per day. Thirteen patients had some dizziness. Four of these had other complications (two, blurring of vision, one, deafness, and one, mild vesicular dermatitis). Of those who did not have

dizziness, only two had complications. One of these had mild blurring of vision and the other an exfoliative dermatitis.

We particularly wish to call your attention to one patient, a 26 year old male, who originally presented a painful lesion of the elbow, which was biopsied and left a draining sinus. The biopsy showed a tuberculosis of the ulna. Subsequently he was observed to have additional tuberculosis of the left humerus, left scapula, and a swollen left knee. This swelling of the knee was prominent and progressed despite rest and a brief period of immobilization in bed. Repeated cultures from aspirated knee joint fluid were positive for mycobacterium tuberculosis. There was marked discomfort, and motion was limited to less than 10 degrees because of pain. At the completion of 120 days of streptomycin therapy, his draining sinus of the elbow had closed, the knee joint had returned to normal size, and he was able to flex it about 80 degrees, and he had gained about 10 pounds in weight. Four months later he had a full range of motion of both knees, no evidence of discomfort, and the affected bone of the ulna, humerus and scapula showed distinct evidence of regeneration of bone and return to normal appearance. Ordinarily, any joint which showed a positive culture of tuberculosis either progressed or ended up as a stiff unyielding joint. This striking improvement suggests that at least in some instances streptomycin will be useful in preservation and restoration of tuberculous joints.

### STREPTOMYCIN THERAPY

**Disadvantages.**—The disadvantages of streptomycin therapy are common to many drugs.

1. Frequency of dosage. Obviously any medication which requires repeated intramuscular injections each day is less pleasant than oral medications, or infrequent dosage. Patients soon become accustomed to daily injections, however, and do not seem too displeased, even after prolonged treatment.

2. The expense and need for hospitalization to administer streptomycin therapy may be minimized by improving production and perhaps by subsidies.

3. Complications and reactions in our series were substantially like those in any other group under streptomycin therapy. They were transient and minimal and did not require cessation of treatment. These included: auditory (tinnitus, vertigo, nystagmus and deafness); dermatologic (transient rashes, herpetic lesions of the mouth, and maculopapular rashes); general (headache, malaise and lassitude).

**Advantages.**—Streptomycin therapy offers the following advantages:

1. Improvement in general attitude and feeling of well-being was



consistent in every patient. At first it was thought that this response of the patient might be due in part to the psychic stimulation of so much attention, and furthermore, a new program usually stimulates the patient's response. However, inasmuch as almost every patient responded in this manner, the factor of psychic stimulation must be considered minimal.

2 A distinct improvement in appetite and a noticeable gain in weight has been the universal rule

3. Where pain has been a factor, it diminished with the beginning of streptomycin therapy and in a comparatively short time became minimal or absent.

4 The patients consistently appeared able to rest better and to sleep with less restlessness and for longer periods.

5. There was always a diminution in exudate and, where sinuses were present, they closed over in a period of sixty days in most instances

6. There was no advance of bone changes such as destruction or osteomalacia

7. When abscesses were present without drainage, they spontaneously receded in most instances

8. There was a diminution in the sedimentation rate

9 There was a reduction of period of hospitalization.

10. Restoration and preservation of joint function was general. There is diminution in amount of joint fluid and associated swelling, reduction of pain, and increased range of motion evidenced unquestionably in one case observed for more than a year

### CONCLUSIONS

1. Cases should be carefully evaluated before therapy.

2 Therapy should be carefully observed throughout its course

3 Streptomycin is not without danger

4 Streptomycin appears to arrest progress of osseous and joint tuberculosis and makes the patient feel better.

5 Streptomycin is not a substitute for surgery, but should rather be considered as a useful adjuvant to the proven principles of tuberculosis therapy (1) tranquility and repose, (2) excellent nutrition, (3) a wise, considerate, and understanding physician, and (4) a high degree of patience

# TOXIC REACTIONS TO STREPTOMYCIN IN PATIENTS WITH PULMONARY TUBERCULOSIS HAVING THORACIC SURGERY

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THE toxic reactions occurring during streptomycin administration have been fully described in previous articles.<sup>1-11</sup> The purpose of this report is to describe toxic reactions encountered during prophylactic streptomycin therapy in a group of patients undergoing surgical treatment of pulmonary tuberculosis, in whom sufficient time has elapsed since completing their therapy to evaluate their clinical status.

The patients studied in this evaluation consisted of thirty cases, meeting bacteriologic and other diagnostic criteria, who were chosen by lot to receive prophylactic streptomycin while undergoing surgical therapy as outlined in the Veterans Administration Streptomycin Surgical Protocol. Twenty-nine of the patients studied had thoracoplasties and one patient had a lobectomy. These patients were treated between February and December of 1947.

There were fourteen patients who manifested toxic reactions sufficiently severe to warrant interruption and/or cessation of therapy. These patients were all in the group of cases given streptomycin prophylactically while undergoing thoracoplasty. The primary toxic symptoms and signs observed in these patients were nausea and vomiting, skin rashes and vertigo. Severe nausea and vomiting were noted in eight patients. Severe skin rashes occurred in three patients; in two the rash was maculopapular in character and in one the skin disturbance was morbilliform and urticarial in nature. Marked vertigo was noted in eleven patients. Eight of these patients presented two of the toxic symptoms or signs mentioned but none presented all three.

Interruption of streptomycin therapy was necessary in eleven of the patients described, and complete cessation of therapy prior to completion of surgery was necessary in nine patients, six of whom were also included in the group whose therapy was interrupted and restarted prior to final cessation.

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Thirteen of the fourteen patients received an initial dose of 2 gm. of streptomycin daily, given in divided doses, and one patient received an initial dose of 1 gm. daily. In six of the patients in whom therapy was interrupted the initial dose was 2 gm. daily and the dosage following interruption was 1 gm. daily; three of these patients were carried to completion of their therapy without cessation on this dosage. A study of the vestibular reaction to caloric stimulation in this group of fourteen patients revealed a diminished vestibular response in twelve patients. This diminished vestibular response was noted four to six weeks after beginning therapy. In all twelve of these patients the vestibular response had returned to normal at the time of this report. This return to normal of the hypofunctioning vestibular nerve occurred four to twelve weeks after cessation of streptomycin therapy. In none of these patients was an appreciable deafness encountered as evidenced by audiometric determinations. In three patients of the prophylactic group who did not show marked toxic reactions, the vestibular response continues to show marked reduction at the time of this report although these patients were able to walk well, experiencing their only difficulty when walking in the dark.

In two patients showing toxic manifestations, coincidental blood changes were also noted. In these patients a clinical course suggestive of infectious mononucleosis was encountered. In addition, transient lymphocytosis and positive heterophil agglutination reactions were present, but these findings cleared with continued streptomycin therapy and did not recur.

There were fifty-eight thoracoplasty operations or stages performed on the fourteen patients considered. A minimum of three stages and a maximum of five stages were performed per patient, an average of  $4\frac{1}{2}$  stages per patient. The time interval between stages varied from two to eight weeks, the average time interval being three weeks. There was no evidence of tuberculous extension or spread noted in any of these patients during this surgery. The causes of operative delay between stages were toxic streptomycin reactions in four patients, a gastric ulcer in one case and infectious mononucleosis in two.

All of the patients in this series were males. The ages of the patients varied from 22 to 58 years, and the average age was  $32\frac{1}{2}$  years. The patients had been observed in these hospitals a minimum of five months to a maximum of two years prior to the beginning of thoracoplasty. The pulmonary lesions observed in this group of patients were variable as to extent and duration but in general they were fibrocavitary in type. There were no serious toxic manifestations of streptomycin other than those described.

## CONCLUSIONS

1. Out of a group of thirty patients to whom streptomycin therapy was given prophylactically in the course of thoracoplasty for pulmonary tuberculosis, fourteen patients were reviewed in whom toxic reactions occurred

2. In this group of patients, eleven required interruption of the streptomycin therapy, and nine required eventual complete cessation of the drug because of the toxic manifestations.

3. It was our impression that toxic reactions to streptomycin were more severe or were less well tolerated in surgical patients than in medical patients

4. Furthermore, it was our impression that toxic reactions to streptomycin were more likely to occur with daily dosage of 2 gm. than with a daily dosage of 1 gm.

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